

More Hopes for Arms Control

THE weeks ahead should provide some sign of which way the wind is blowing on disarmament. The next round of the SALT (Strategic Arms Limitation Treaty) talks will open on November 21 and the following day there will be the first session of a meeting of ambassadors at Helsinki to work out an agenda for the European Security Conference promised for some time in 1973. The meeting at Helsinki will no doubt clear the ground for the first meetings of the proposed conference on the "mutual and balanced reduction of forces" (MBFR), regarded by the governments of Western Europe as a necessary preliminary for the conference on European security but which are likely to become as protracted as the SALT talks themselves. To be sure, China remains obdurately convinced that the only equitable forum for discussions of international disarmament must be strictly international, and that hobnobbing with other members of the nuclear club is not permissible, even when measures of arms control are on the agenda, but China does now at least belong to the United Nations and has become conspicuous on the itineraries of heads of government.

With all this said, it would be wrong to underestimate the outstanding difficulties of the SALT negotiations. The agreements signed in Moscow in May between the United States and the Soviet Union are still imprecise, and the first task at the new SALT meeting will be to appoint the standing commission which is supposed to supervise the working of the Anti-Ballistic Missile Treaty. This is a complicated matter because the ABM treaty is full of technical definitions which will require continual redefinition. The treaty says that each nation must have no more than two ABM deployment areas, each no larger than 300 km in diameter and equipped with fewer than 100 ABM launchers and missiles. In practice this means that the Soviet Union would be free to strengthen its system around Moscow and to develop another ABM launching area, no doubt in the neighbourhood of its ICBM launching sites. The United States will be free to complete the ABM site chosen at Grand Forks, North Dakota, but will have to abandon the other sites originally selected for the Safeguard system but will have the option, in the years ahead, to provide an ABM defence for Washington, DC (for the treaty says that one of the two permitted ABM sites must surround the national capital). The difficulties of interpretation arise over those clauses in the ABM agreement which prohibit the testing of other kinds of missiles in what is called the "ABM mode" and the deployment of radar systems which could be used as components in an ABM defence—there are ways in which the development of space tracking networks or even air traffic control systems might be held to be breaches of the agreement. There are also possibilities that novel technological developments—laser systems, for example—might be held to break the agreement. In any case, the ABM treaty implicitly assumes that each partner will attempt to monitor the other's performance by means of surveillance satellites and even old-fashioned espionage, and there is obviously plenty

of room for argument about the interpretation of the results of such activities. In all the circumstances, the standing commission will need to be diplomatically subtle and robust.

The interim agreement on offensive missiles, also signed in Moscow in May, is much less complete than the agreement on ABMs. The principle of the agreement, which is to run for five years from the ratification of the ABM agreement, is that the number of land-based ICBM launching sites in existence or under construction on July 1 this year should not be added to, but both parties are free to replace outdated missiles with more modern rockets provided that these are not "heavy" ICBMs of the kind typified by the Soviet SS-9. The interim agreement also limits the number of rocket-launching submarines to the numbers under construction or in service on July 1 this year, but there are provisions that would allow the United States to exchange some land-based launching sites for submarine launchers. It is by no means clear what the interim agreement implies for the strategic balance between the two sides. The United States has 1,054 land-based rockets and 656 Polaris and Poseidon missiles in 41 submarines. On paper, the Soviet Union is in a stronger position, with 1,618 land-based missile launchers and 740 submarine rockets, some of which are carried by diesel submarines. One imprecision in the interim agreement is the precise meaning of the term "under construction"—will the Soviet Union be able to argue that it should be allowed to dig holes in the ground to accommodate equipment now being manufactured? And what in any case is to be done about heavy aircraft, not covered by the agreement but still an important part of the strategic forces of both countries? It is hard for outsiders to know whether the figures implied by the interim agreement are equitable—the numerical superiority accorded to the Soviet Union in launchers and the fact that more than 300 SS-9 rockets, each carrying a warhead of 25 megatons, may be cancelled out by the multiple warheads fitted or being fitted to the Minuteman 3 rocket (which has three separate warheads) and to Poseidon (which can carry up to ten warheads), and no doubt the SALT negotiators will wish to keep talking on subjects like this. In the circumstances, what else can they hope to achieve?

The first thing to say is that to keep on talking is a desirable end in itself. Nobody should complain if several months go by before the negotiating teams are able to take up the more contentious issue of a reduction of the existing levels of offensive strategic weapons. Moreover, because the deployment of multiple warheads can always in principle make up for a reduction of the agreed numbers of launching sites, there is little reason to suspect that reductions of the numbers of permitted launching sites would entail effective reductions of offensive power (even though one result might be a welcome economy of cost). Yet both sides are now equipped with more than enough strategic power to ensure that they could make an overwhelming response to a strategic



attack, which is why it is important that they should at least aim at a further tightening of their reciprocal self-restraint on the deployment of strategic weapons. Since the existing forces, by their mere existence, are not, however, a threat to international stability, the best course will be to look for formulae by means of which the two countries can avoid expenditure on the development of yet another generation of missiles and the continuing expense of keeping strategic aircraft in service. By the end of the decade, the result could be a substantial attrition of the strategic forces. For the rest, SALT negotiators should look for other directions in which to make progress. Schemes for agreements not to deploy multiple warheads are beguiling but probably impractical. The best hope is by an extension of the partial test-ban to include underground tests, which is why at some point the two powers will have to agree that they must talk to the Chinese. It goes without saying, however, that unless something can be done before the natural expiry of the interim agreement five years from now to make it more effective, its beneficial consequences will evaporate.

This is why the talks on European security and the balanced reduction of European forces are relevant. Although the forces, men and weapons, now deployed in Eastern and Western Europe are if anything on the decline, they are probably more than are strictly necessary to match the military needs of the two alliances. The European command of NATO has some 7,000 tactical nuclear warheads at its disposal. The nuclear arrangements of the Warsaw Pact countries are not apparent but there are many short-range missiles deployed, while missiles with longer range based in western parts of the Soviet Union are obviously relevant to the defence of Eastern Europe. At least for the West, the deployment of tactical nuclear weapons (many of which are more than the equivalent of 100 kilotons of TNT) is an important economy of manpower, but it is also clear that the danger in conventionally mounted attacks by one side on the other would now be much more hazardous because of the substantial improvements that there have been in anti-tank technology. So is it not reasonable that the MBFR talks should concentrate first of all on a definition of those kinds of weapons, heavy tanks for example, which might play a part in conventional attacks, then on an agreement to restrict the numbers of these that may be sited within, say, 200 km of the border between East and West Germany and, finally, on an attempt to exclude nuclear warheads altogether from such a zone? Undoubtedly the conversations will raise all kinds of formal political problems. Many would ask about the security of West Berlin. There would be problems in winning the collaboration of France, which would necessarily have to accommodate some of the material displaced from West Germany, and even anxieties on the part of the Soviet Union about the extent to which steps towards arms limitation in central Europe would loosen its central control of the Warsaw Pact. All this implies that the talks must necessarily be long and if anything more contentious than the SALT negotiations. It is unthinkable that they could succeed without agreements between the members of the European Community about the directions to be followed in working out a common European defence policy. In the House of Lords on November 1, Lord Carrington was as pragmatic

as anybody could have been on this question, but the need to begin talking about a common defence policy is urgent, not merely because of the economies it might bring but because the lack of an understanding may soon become an impediment to valuable agreements on arms control.

Money for Communications

THE British Post Office, although in theory an independent entity required to operate on commercial principles even though wholly owned by the British government, has just survived its periodical application to the British parliament for permission to borrow extra sums of money. The Post Office estimates that in the next five years it will need to invest £4,000 million in new equipment, most of it for telecommunications, and on current arrangements half of this will be paid for by depreciation and internal savings and half will be loaned from public funds. In the debate in the House of Commons last Friday on the Post Office (Borrowing) Bill, there appeared to be no dissent from the view of Sir John Eden, Minister of Posts and Telecommunications, that rapid investment in better telecommunications is an urgent national need, and that is as it should be. But there are serious questions about the wisdom of the present arrangements for regulating the relationship of the Post Office Corporation with the government and with the House of Commons. There are also questions to be asked about the Post Office Corporation's commercial policy, many of which were unanswered by last week's debate.

Now that the Post Office Corporation has ceased to be a government department, parochial questions about the delivery of mail in particular London suburbs or the Scottish highlands are no longer asked, and that is as it should be. But the British parliament, in theory at least the representative of the taxpayers who finance the development of the Post Office as well as of the Corporation's customers, is inadequately supplied with technical information about the corporation's investment plans. The glossy prospectus with which the Post Office Corporation marked the publication of the government's bill says nothing about the alternative investment strategies which might have been followed and which have presumably been rejected in discussions with the government. Moreover, this document is argued exclusively in terms of providing a better service in the immediate future—the Post Office wishes to reduce its waiting list for telephones (at present 220,000), to improve the working of the telecommunications system for those already connected to it and, no doubt, to lay foundations for a more radical reconstruction of the trunk network in the 1980s. All this is worthy, and even overdue. What the Post Office has now argued is that an investment of £800 million a year, mostly on equipment of the kind now in service, will bring a vast increase of its business (at present growing at such a rate that it multiplies by two each decade) which, in turn, will enable it to afford the extra £200 million a year which, on the average, it will have to contribute to its own capital investment in the next five years. Especially because the current price freeze will restrict its capacity to put up prices, there is at least a chance that its calculations will be falsified by events. Those members of parliament who asked

last week for a fuller and more technical justification of these points are entirely in the right.

What of the more distant future? The Post Office is already the most prolific investor of all the British nationalized industries—the nearest competitor, the electricity industry, is now making do with just over £400 million a year. But in the 1980s, the Post Office will surpass its present performance, for then there will be an urgent need to build a new high capacity trunk network and to begin work on the provision of digital communications to subscribers of all kinds. A decade from now, the complaint will be that the Post Office has not invested sufficiently in wide-band links for business and even domestic subscribers and that its capacity to do so is restricted by the technical character of the exchange equipment still being installed or soon to be installed. It is not therefore entirely impolite to ask whether there might not be advantages in postponing some of the development now planned for the sake of the chance to invest in still more powerful and presumably profitable equipment ten years from now. It is true that such a strategy would imply a less rapid improvement of the telecommunications network than now seems likely, but it is at least an option that deserves some public discussion by the shareholders. It is also proper, if openly impolite, to ask whether the Post Office Corporation could have sustained its present programme of development with equipment bought off the shelf from suppliers on the mainland of Europe. There is at least a suspicion that the old chauvinism lingers on.

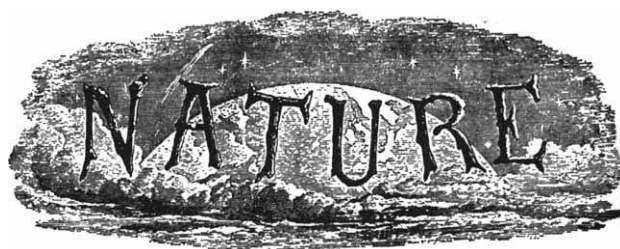
The House of Commons is also well placed to ask some searching questions about the Post Office Corporation's relations with its customers. Britain is distinguished from other industrial nations by the small percentage of telephones in use which belong to personal as distinct from business subscribers and by the poor usage of telephones by private customers. By all accounts, the corporation would like to see these habits changed but has not been especially vigorous in its attempts to change them. There are quite substantial charges to be paid by those who ask for the privilege to become telephone subscribers when thoroughly commercial operators would seek to recover the costs of installing new telephones and telephone lines from the business that they would generate. And there are charges made for even the first calls made in every quarter when an out-and-out commercial policy aimed at a fuller use of the capital investment would lump a free quota of calls in with the usual rental fee. And little has been heard, in Britain, of the use of the telephone system as a social service although it has been recognized elsewhere, in New York for example, that old people and the sick are even more urgently in need of access to a telephone than the well-to-do. These again are issues on which the House of Commons deserves a detailed explanation. Sir John Eden should provide it.

Inners and Outers

PROFESSOR HERMAN BONDI's committee on the mobility of scientists between government departments on the one hand and industry and the universities on the other (see page 120) is entirely laudable, but neither he nor his wellwishers should be disappointed if very little is

achieved. The Fulton commission on the civil service, now four years old, did much to dramatize the need for mobility of this kind, and there is no doubt much that could be done to remove the impediments which at present restrict the movement of people. To set out, as Professor Bondi has done, to make pension rights transferable, both for those who leave the civil service and those who enter it for short periods, is a necessary first step. But if the object of Professor Bondi's exercise is to make it seem attractive to gifted people to take up short commissions in the civil service, much more than this will be needed. The experience of the Administration in the United States is a good illustration of what is necessary. The enlivenment of the United States government by the steady stream of enterprising people from outside now envied by the Civil Service Department is possible only because people joining the United States government for short periods can hope that they will nevertheless be able to do a tangible and useful job and in the process wield political influence of a sort. In the British government's attempt to strengthen the Chief Scientists' organizations of government departments, it is clear that there will be many potential openings of this kind. But is there any chance that the civil service will allow these to be posts in which scientists from outside might feel free to act constructively?

100 Years Ago



MR. BESSEMER'S SALOON STEAMER FOR THE CHANNEL PASSAGE

THE prevention of sea-sickness by means of a swinging cabin has nothing novel about it, but the originality and inventive merit in the suspended saloon devised by Mr. Bessemer, and now about to be actually constructed in a ship specially designed for it by Mr. Reed, the late Chief Constructor of the Navy, are of the highest order. The association of those names is in itself a sufficient guarantee that the idea will be carried into execution with complete security as respects the safety of the passengers and the seaworthiness of the ship, and a full knowledge of the scientific principles involved.

On the whole, while we are unwilling to commit ourselves to any prophecy, either of complete success or of partial failure, we think very favourably of the proposal. As a mere scientific experiment it is one of the very highest interest. As a practical design it offers a sure prospect of realising a large part of its intention, and a fair prospect of attaining a high degree of success. We feel confident that it will save a great many who would otherwise suffer, from being sea-sick at all, but we can hardly hope that there will not be sufficient residual motion in very heavy weather to cause some degree of uneasiness to very sensitive persons; nor would we venture to predict what will be the numerical reduction in the proportion of persons relieved from sickness, or the amount of alleviation to those not wholly saved from it.

From *Nature*, 7, 41 and 42, November 21, 1872.

OLD WORLD

Agreement Reached on Dumping at Sea

AN international convention to prevent the dumping of waste at sea has been agreed in London. Following a two-week meeting, 57 of the 91 countries in attendance have so far initialled an agreement which prevents the dumping of persistent and toxic wastes and ties the dumping of less toxic wastes to a permit system.

The substances that can no longer be dumped at sea include organohalogen compounds, mercury and cadmium and their compounds, persistent synthetic materials, high level radioactive wastes and substances produced for chemical and biological warfare. A second class of substances, including most heavy metals, cyanides, fluorides, pesticides, low level radioactive wastes and bulky objects that might endanger navigation or fishing may be dumped only when a special permit has been obtained, and general permits can be issued to permit the dumping of substances that the sea can render harmless — for example sewage sludge.

Mr Eldon Griffiths, Under-Secretary of State at the Department of the Environment, described the pact as "an important step forward in control", and Dr Martin Holdgate, head of the Department of the Environment's pollution unit and chairman of the conference, said that he was pleased with the "genuine wish for agreement and consensus" among the countries attending. All the leading maritime powers have signed the pact, other countries are expected to sign and it is thought that China may well be among these.

But not everyone will be happy with the convention as it now stands. Agreement was not easy to achieve—the conference overran by three days and at one point almost broke down—partly because of fears that the convention might prejudice the United Nations Law of the Sea Conference planned for next year. As a result there is a clause specifically stating that the convention does not prejudice that conference, but, as a result, there is no direct provision for enforcing the agreement. Meetings will have to be held next year to discuss the operation and policing of the pact. There is little in the convention as it stands to satisfy the hopes of Mr Peter Walker that the conference would agree methods of detection and enforcement.

Nevertheless, the convention is a clear declaration of intent, for whatever that may be worth. It includes provision for

regional agreements to limit dumping still further (on the model of the recent Oslo convention to which Britain is a signatory), and provides for meetings to devise procedures for settling disputes concerning the interpretation and application of the convention. It also makes each country responsible for ensuring that ships bearing its flag, and all ships using its ports, are not planning to infringe the agreement. Mr Eldon Griffiths clearly feels that this alone will do much to ensure that the convention is executed. It will, he said, cover 98 per cent of the cases of dumping. On the effect of the convention on ships operating from British ports, however, Mr Griffiths admitted that the convention is no great stride forward. "I do not think that the convention of itself will place on British industrialists any obligation which we do not already

expect them to carry out," he said.

The convention is open for signature for a year from December 29, 1972, and will come into force when fifteen countries have ratified it — probably about the middle of 1973. The only notable omissions from the list of those who have already initialled the agreement, are Liberia and South Africa, but their omission does not necessarily mean that they will not sign in the near future.

The convention covers all intentional dumping at sea, but does not include the disposal of waste from vessels or aircraft if such disposal is derived from their normal operations. Waste arising from off-shore exploration and exploitation of mineral resources is not covered, and warships and military aircraft are also exempt from the convention's provisions, although

CIVIL SERVICE

Mobility of Scientists

PROFESSOR Herman Bondi's task force on the interchange of scientists, set up in August, demonstrated last week that it means business. The task force has already started discussions with industry, universities, civil service and research councils on the mechanics of transferring scientists, and the task force hopes to arrange its first moves before the end of the year.

The task force is trying to emulate the system in the United States where it is quite common for scientists to move in between industry, university and government with immense benefit to society and employers without being detrimental to the career of the scientist.

In Britain, movement of scientists has, in the past, tended to be at the more senior levels and the aim of Professor Bondi's task force is to widen the horizons of first class scientists in their thirties by transferring them for periods of up to three years to a new location but interesting them in work of a different character from that which they had been doing before.

Professor Bondi hopes that his task force will be able to arrange the move of some two to three dozen scientists in the next year but there are no plans to keep the force permanently in existence. By next summer Professor Bondi hopes that the scheme will have had enough of an impetus for it to carry on

unaided under its own momentum.

The aim of the task force is to act as brokers for the move of scientists from one job to another. The Civil Service Department is ensuring that a man's pension rights are not affected by any move while the task force is establishing with employers that any person seconded will not lose his place in the promotion queue. The task force is spending part of its time on acquiring an understanding of the obstacles which face anyone moving from one job to another.

Professor Bondi said last week that he hoped that some of the temporary transfers would turn out to be permanent and he hoped that mobility not only in the sciences would become more a part of life in Britain.

Severe reservations as to the success of the scheme were voiced at the third Universities Conference held last week. There was a feeling that any scientist who opted out of the university system for several years would not be able to regain his place on the academic ladder. A suggestion was made that a talented person such as Professor Bondi envisaged taking part in the scheme could be awarded a chair before he left university for other pastures so that his academic future was ensured. Similarly it is difficult to see industrial employers readily parting with their top people even though under the scheme they would probably play host to a university or civil service person for the same time.

the ratifying countries agree to keep their military activities within the spirit of the pact. In this connexion, it is noteworthy that products for biological and chemical warfare may no longer be dumped at sea.

Whereas the convention may not be all Mr Peter Walker hoped it would be before he left the Department of the Environment for the Department of Trade and Industry, it does at least include in its first article recognition that dumping at sea is not the only (or indeed the prime) source of sea pollution. The convention recognizes that "all sources of pollution" must be controlled, and Mr Griffiths is adamant that "a world clean rivers programme must be the next step."

UNIVERSITIES

Radical Reorganization

A WHOLESALE reorganization of the colleges of the University of London is recommended this week by Lord Murray's commission of inquiry into the governance of the university (*Final Report of the Committee of Enquiry into the Governance of the University of London*, University of London, 1972). The commission would have King's College and University College apply for independent charters and would amalgamate Bedford College, Queen Elizabeth College, the Royal Holloway College and Westfield College, both physically and academically. Wye College, in spite of its wish to remain a part of the University of London, should consider transferring to the University of Kent if "there were a major development of the biological sciences" there. The commission also suggests a reorganization of the medical schools and institutes along the lines recommended by Lord Todd's Commission on Medical Education.

Lord Murray also recommends that Imperial College should lose the special status it holds by which the UGC grant to the college is specially earmarked. During the year ending on July 31, 1973, the University of London will receive £54 million from the UGC and Imperial College will be allocated £7.5 million of this. This income arrangement will continue until the present UGC quinquennium ends in 1977. Thereafter, the committee recommends that no such special allocation be made to Imperial College and that it should be treated on the same basis as any other colleges of the university.

King's College and University College have been part of the university since the early 1900s when they gave up their independent status. The committee considers that the inclusion of these colleges in the university has

become anomalous "and in real life meaningless" and that they should revert to their former independence.

The committee comes down firmly against smaller colleges on the grounds that they cannot be administratively and academically viable. Small specialized schools, according to the report, will find it increasingly difficult in future "on the basis of their own unaided resources to keep up with new developments and the progress of interdisciplinary teaching and research in the area of their work". Small multi-faculty schools will similarly find it difficult to support many disciplines while building up individual departments—especially in the sciences.

The small schools are at a disadvantage compared to the larger schools in attracting first class candidates in the sciences—but not in the arts. They also receive fewer first choice candidates for undergraduate places in both arts and sciences and the figures for 1970 and 1971 show that the small colleges of the university accepted only 67 per cent of the first, second and third choice candidates for places at these colleges compared with the larger colleges which accepted 8 per cent of these candidates.

In certain cases the committee thinks that a wholesale "surgical operation" is called for with sites being sold and the colleges being physically regrouped to produce a viable larger college. "Traditions of independence may have to be sacrificed in order to achieve greater academic strength and opportunities for academic growth."

Lord Murray suggests several possibilities for amalgamating the small colleges. Bedford, Queen Elizabeth and Westfield Colleges could be fused to produce a "multi-faculty complex of great academic strength and potentiality". This trinity, says the report, could also be associated with a combination of the medical schools of Middlesex and St Mary's. Royal Holloway should be doubled in size or one of the other colleges should be moved out to join it in Surrey to make an academically viable unit.

The committee is broadly in favour of the reorganization of the medical schools and their association with colleges of the university according to the current university plans. Lord Murray also agrees with the current university plan to accord independent status to the British Postgraduate Medical School. The report recommends, however, that the Lister Institute of Preventive Medicine should lose its status of a school of the university as it is essentially a research institute and does no undergraduate teaching. The committee points out that postgraduate students of the institute will still be able to read

for University of London doctorates. The institute, says the report, could if it wanted to then seek an association with one of the medical schools. The future of the London School of Hygiene and Tropical Medicine is also being currently discussed within the university and Lord Murray hopes that the school can develop an appropriate association within the spirit of the recommendations of Lord Todd's Commission.

NUTRITION

Annual Award

SIR RUDOLPH PETERS has been awarded this year's British Nutrition Foundation prize of £1,000. Sir Rudolph, one-time Whitley professor of biochemistry at the University of Oxford, who has continued research since then, first at the Institute of Animal Physiology at Babraham and then at the Department of Biochemistry at the University of Cambridge, addressed the foundation last week on "The Neglect of Nutrition and its Perils".

The discovery of vitamins and the elucidation of their metabolic roles in the years before the war placed nutrition in the forefront of the scientific field but it has declined in popularity since then, said Sir Rudolph. He deplored the relatively low status of nutrition as a scientific subject, which has tended to direct young research workers into the more fashionable fields of biochemistry, and he pointed out that the excellent enzyme studies of recent years had hardly been extended to consider their roles in the body.

Sir Rudolph's own work clearly shows the essential connexions between basic research and its applications. His early work on enzyme chemistry and the biochemical basis of thiamine deficiency led to his developing antidotes for poison gases containing arsenic, which in turn developed into an interest in fluoride metabolism and nutrition. Sir Rudolph stressed that in his own work many paths had led eventually to problems of nutrition, and that recent work on hitherto unsuspected trace element requirements showed that continued support for nutritional research was essential.

The British Nutrition Foundation is financed by most of the major companies in the food industry. Membership has up to now been restricted to organizations involved in food manufacture and research, but a resolution passed at the annual general meeting last week now opens membership to those involved in the education and information media. The foundation aims to finance research and education in nutrition and last year gave £28,000 in research grants.

SPACE

Progress at Last

A EUROPEAN Space Agency is the one constructive suggestion to emerge from last week's meeting of European aerospace ministers in Paris. Mr Michael Heseltine, Minister for Aerospace, confirmed in the House of Commons this week that he had proposed the creation of such an agency to handle the £200 million that Europe spends on space each year.

If adopted—and it is understood that both the French and Germans reacted favourably—the agency could go some way to sorting out the fragmented chaos of Europe's space activities. In effect the agency would be responsible for running all the space projects that come under the European Launcher Development Organization (of which Britain is no longer a member) and the European Space Research Organization, and for running each country's national programme. Britain is willing to put all her space activities except her international commitment to Intelsat and her Skynet military programme under the agency's control, making Britain's commitment to the agency worth about £20 million.

The agency would also be responsible for any European involvement in the post-Apollo project. The British attitude is understood to be that Britain should not consider partaking in the post-Apollo programme in isolation as this will only contribute further to the piecemeal approach to space that has characterized Europe's efforts in the past. If a space agency comes into existence, then Britain will consider joining a post-Apollo programme through the agency.

Organizational details of the proposal have still to be worked out, but one of the key points in the idea is that each nation would put only those space activities it wanted to under the agency's control, and the financial contribution of each country to the agency would be based on the projects it wished to support and not on a levy related to gross national product. This would, for example, allow Britain to partake in most European space projects but would not force her into an involvement with a European launcher.

The British thinking is that if the agency could be created, Europe's £200 million expenditure on space might begin to achieve a just proportion of the results that the United States achieves with its £1,000 million a year.

As a result of the Paris talks, a full meeting of the European Space Conference is now planned for next month—the last two meetings having been cancelled—when a more detailed version of the proposal will be presented.

Following last week's meeting the

ESRO council decided that phase B of the industrial studies for the post-Apollo sortie laboratory should go ahead. West Germany (which of all the European nations appears most eager to join in the post-Apollo programme), Belgium, Italy and Spain have indicated that they are willing to finance this stage of the studies; other member states of ESRO have been invited to join them.

RESEARCH AND DEVELOPMENT

University Science

THE effect of transferring some £20 million a year from the research councils to government departments will depend critically on the extent to which a sense of partnership can be built up. So said Sir Frederick Dainton at the third Universities' Conference, held at Imperial College last week under the auspices of the Committee of Vice-Chancellors and Principals and the Association of University Teachers (AUT). Sir Frederick's view was reiterated, albeit from the other side of the fence, by Professor Herman Bondi, Chief Scientific Adviser at the Ministry of Defence.

Sir Frederick said that many academics have little feeling for the global sums that come to the universities from the research councils. As a consequence a substantial part of his address was essentially didactic, and dealt with the changes during the past twenty years that have led to the situation summarized in the Table. Turning his attention to the future, he declined to "do the impossible" by justifying the £20 million which is eventually to accrue to government departments at the expense of the research councils. The now defunct Council for Scientific Policy, he said, was of the opinion that the amount involved should be more like £8 million. Whether or not the contracts meted out to the research councils

by government departments would make up the shortfall in the money directly available to them will, in no small way, be determined by the extent to which the new Advisory Board for the Research Councils becomes "an effective forum" and can deal with the financial complexities that are bound to be involved, said Sir Frederick.

In an account of the place of university research in the University Grants Committee planning, Sir Robert Aitken, deputy chairman of the UGC, said that the committee in no sense attempts to "identify a teaching component and a research component and add them together". But a university that decides to use more of its general funds for research is really diverting money away from teaching and *vice versa*. Sir Robert did, however, warn that although the UGC "has hitherto been able to provide accommodation for research supported by research councils . . . it is becoming doubtful how far it can continue to do so".

Professor Bondi repeated his call for more interchange between the universities and Whitehall (see page 120) to ensure that the chief scientist organizations in government departments are both well informed and respected by the scientific community. Professor Bondi did, however, admit that the potential problems were great. Professor H. J. Perkin, vice-president of the AUT, wondered how quickly "outlook can be changed with the hat".

Mr J. E. Reilly, assistant registrar at the University of Kent, summed up the misgivings of several participants in the conference when he asked whether smaller universities and departments would get a fair share of the research commissioned by government departments. Professor Bondi said that no problems would arise provided that smaller departments do not try to ape the larger ones in their choice of research topics.

Estimated expenditure of the Research Councils, 1971-72

	Science Research Council	Social Science Research Council	Medical Research Council	Agricultural Research Council	Natural Environment Research Council
	£ million				
Research grants to universities	11.3	1.7	5.8	0.8	1.2
Training awards and research training support grants	6.0	2.0	0.8	0.1 †	0.72
Post-doctoral fellowships	0.4	0.05	0.3	—	0.03
Research units and external staff	Small	0.13	9.3	6.2	—
Own establishments and national facilities	21.0	—	4.9		11.6
Grant aid to institutions	—	—	1.4	11.5	1.4
International subscriptions	13.7 *	—	0.1 †	—	—
	52.4	3.88	22.6	18.6	14.95

*Grants to CERN (£8.2 million), ESRO (£5.1 million) and NATO (£0.4 million).

†International Cancer Agency. ‡Includes equipment; training awards to postgraduate students in agriculture are made by the Ministry of Agriculture, Fisheries and Food (£0.1 million).

NEW WORLD

Recipe for Stability

by our Washington Correspondent

How can American universities find a measure of financial stability? There can be few scientists in the United States who are unaware of the problems caused by financial constraints during the past few years. Yet graduate production continues apace, the job market cannot accommodate those who have already left the universities, important scientific facilities such as the high energy accelerators are being operated at less than full capacity and there is little chance of an improvement in sight. Last week, however, the Federation of American Scientists published a report* which suggests a few steps that the scientific community itself could take to alleviate the situation. Many of the suggestions are familiar, many are controversial and most would change much of the traditional way of going about research in the universities.

Much of the federation's case rests on the contention that "the American scientific establishment is high in quality and is about the right size for the size of the economy, the present development of technology and the natural momenta of the disciplines themselves". This suggestion leads the authors of the report—Francis Low, Herman Feshbach and Jeffrey Steinfeld of MIT and Joel Primack of Harvard—to recommend that "university research establishments cannot be justified primarily on the ground of training professionals".

The report points out that the present oversupply of graduate scientists is partly a consequence of the fact that it takes about eight years to train a professional scientist, while fluctuations in demand take place over a much shorter time scale. Moreover, the Vietnam war and the anti-inflationary policies of the Administration have coincided with peak output from the graduate schools. But a change in federal funding policies, coupled with "a more thorough and thoughtful reordering of national priorities, could very well reverse the present trend". Although they do not come right out and say it, the authors of the report are suggesting a similar approach to science funding to that contained in Senator Kennedy's National Science Policy and Priorities Act.

What they are suggesting is, first, that scientists in university research departments should take stock of what they are doing. Graduate education must

seek to train students who will not necessarily become research assistants; PhD courses should be broadened and made more flexible—the present PhD "represents a degree of specialization inappropriate for many careers in industry and teaching, and sometimes unsuitable even for pure research"—and thought should be given to establishing a level of training that does not go as far as the PhD. In any case, universities should "at least be circumspect in such matters as inaugurating new graduate programs or expanding their faculties along the traditional lines".

The authors of the report eschew the idea, however, of divorcing scientific research from education, but they do fly a kite by suggesting that the United States should follow in the footsteps of British higher education by building up "centres of excellence" in a few universities instead of spreading research money thinly. "Perhaps a few universities should be designated 'National Universities' and be given broad and secure institutional support, and regional responsibilities," the authors suggest.

PIONEER 10

So Far, So Good

by our Washington Correspondent

PIONEER-10, which is *en route* to a rendezvous with Jupiter in December next year, has successfully traversed half the asteroid belt that lies outside the orbit of Mars and, according to project officials, should have little difficulty crossing the rest. Preliminary data sent back from particle detectors and telescopes aboard the spacecraft have, however, led to suggestions that the belt has some rather surprising features.

One experiment, which measures the rate at which tiny dust particles ranging between 0.01 and 0.1 mm impinge on the spacecraft, has found that the number of particles has remained approximately constant since launch, and has not increased, as expected, in the asteroid belt. The detectors, which consist of 234 gas-filled cells, have been punctured by 83 particles so far. The expectation was that the rate of impact would diminish as the spacecraft left near-Earth space, then increase ten-fold as it entered the asteroid belt.

According to Dr William Kinard, who is in charge of the experiment, the finding seems to suggest that the dust particles have a common origin, prob-

ably cometary debris, although he said he "had expected to see cometary particles early in the mission and asteroidal particles in the belt". One bonus from the low rate of impact in the asteroid belt is that the experiment will be able to relay back data for a much longer period of time.

At the same time, however, stability of funding should be a primary consideration. The federation seeks to avoid the circumstances of the past few years, in which the US science budget has fluctuated widely. As a first step, the authors of the report suggest that the Office of Management and Budget should make public its detailed five-year projections, which could then be further clarified by the individual funding agencies. Publishing five-year projections would not, however, avoid the circumstances in which the Office of Management and Budget often withholds appropriated funds because of short-term fiscal constraints. Such a process is going on this year, for example, for the OMB has now withheld the extra funds Congress had earmarked for the Atomic Energy Commission. The report has no answers to that problem.

Although much of what the report has to say has been heard before, the federation said last week that the necessity for rethinking graduate education has not permeated to all levels of US higher education. The report itself was prepared by members of two of

ably cometary debris, although he said he "had expected to see cometary particles early in the mission and asteroidal particles in the belt". One bonus from the low rate of impact in the asteroid belt is that the experiment will be able to relay back data for a much longer period of time.

A second experiment, which consists of four telescopes aboard the spacecraft, has found the number of larger particles in the asteroid belt to be rather higher than predicted. So far the telescopes have picked up sightings of between 100 and 200 particles greater than 0.1 mm (the telescopes can detect a 0.5 mm particle from a distance of 10 metres). There is a considerable delay in processing the data from the telescope experiment because of its complexity, hence the uncertainty in the number of sightings.

The number of sightings increased as the spacecraft passed through one region of known high density of asteroids which are visible from Earth. Another such region still lies ahead of Pioneer-10, but according to Dr Robert Soberman, who is in charge of the telescope experiment, although the number of asteroids seems to be higher than expected, it is still too low to present much of a hazard to the spacecraft.

*Science, Technology and Education, available from the FAS, 203 C Street NE, Washington DC 20002.

the principal scientific institutions in the United States, however, and the chances that it will filter down to the less prestigious institutions, to which many of its recommendations are addressed, are slim.

CONGRESS

Electoral Fallout

by our Washington Correspondent

ALTHOUGH the Democrats will retain control of the Senate and the House of Representatives when Congress convenes in January, last week's elections left their mark on scientific activities in Congress. The newly created board of the Office of Technology Assessment is particularly affected; two of its members were not re-elected to Congress, and the House Committee on Science and Astronautics, not only lost its chairman, George P. Miller, because a primary election went against him earlier this year, but also lost a senior Democrat in last week's election. Changes will also take place at the top of the Senate Committee on Science and Astronautics, whose chairman, Clinton P. Anderson, has retired.

The OTA board will lose the services of Senator Gordon Allott, a conservative Republican who was surprisingly beaten in Colorado by his Democratic challenger Floyd K. Haskell—a former Republican who changed sides after the Cambodia invasion. Also missing from the OTA board will be Earle Cabell, a Democrat who was defeated in Texas. Cabell is also the second ranking member of the Subcommittee on Science, Research and Development of the House Committee on Science and Astronautics.

The electoral winds did, however, blow more favourably for some members of Congress who are concerned with scientific affairs. John W. Davis, Chairman of the House Subcommittee on Science, Research and Development, successfully fought off a conservative challenger in Georgia, and Mike McCormack, the only former scientist in Congress, won re-election in Washington State. His chances were considered to hang in the balance, particularly since his election to Congress two years ago depended partly on the long coat-tails of Senator Jackson who was then running for re-election as Senator from Washington.

Committee assignments will be sorted out in the next few weeks, before Congress reconvenes in January, but at present the odds seem in favour of Olin E. Teague of Texas assuming control of the House Committee on Science and Astronautics and of Senator Stuart Symington taking the chairmanship of the companion committee in

the Senate. It is also likely that Senator Proxmire and Edward P. Boland of Massachusetts will keep control of the Appropriations subcommittees which decide the budgets of NASA and the National Science Foundation. Between now and January, however, several defections from the House Committee on Science and Astronautics are likely—the committee is no longer the showplace it once was, and some members have not shown their faces at meetings this year.

OCEANOGRAPHY

Diving Off Azores

by our Washington Correspondent

THE National Oceanic and Atmospheric Administration announced this week that a major study of part of the Mid-Atlantic Ridge is to be undertaken with submersibles from France and the United States. The study will consist of some forty dives in a three-year period beginning in the summer of 1974, the object being to map a region of the ridge 200 miles south of the Azores, collect bottom samples and place instruments on the ocean floor. The announcement is a sign that manned undersea research, after a period of quiescence in the United States during which a number of costly submersibles have been mothballed, is being revived.

The submersible study of the Mid-Atlantic Ridge, called the French-American Mid-Ocean Undersea Study (which just happens to have the acronym FAMOUS), is part of a plan recommended by an international group of scientists which met at Princeton in January this year under the sponsorship of the National Academy of Sciences and the US office of the International Decade of Ocean Exploration. The site south of the Azores was chosen, according to Dr George Keller, Director of NOAA's Marine Geology and Geophysics Laboratory in Miami and joint leader of the American part of the study, because it is an area of major spreading which is also cut by a large fracture zone. The location also meets the criteria of good weather and closeness of land for refurbishing.

After further site survey by a research vessel from Woods Hole and by *Discovery*, the British oceanographic research vessel, submersibles will start diving in the summer of 1974. The French submersibles *Archimede* and *SP-3000* and the US vessel *Alvin* will be used. The chief advantage of taking samples by submersibles rather than by coring is that it is possible to record exactly where they come from. Samples will be taken sequentially along the fracture zone, and the chief objective will be to gain a better understanding of the process of ocean floor generation.

Short Notes

Cementing the Link

THE close but informal relationship that has been built up between the Smithsonian Astrophysical Observatory and the Harvard College Observatory during the past two decades will become a little more formal next year. Dr Fred L. Whipple, Director of the Smithsonian observatory since it moved to Massachusetts in 1955, is to retire on July 1, 1973, and he will be succeeded by Dr George B. Field. Dr Field is also Director of the Harvard College Observatory. Dr Whipple will devote his time to research after his retirement, and he will become a Smithsonian Senior Scientist. He will also continue as Phillips Professor of Astronomy at Harvard.

New Thermonuclear Research Chief

DR ROBERT L. HIRSCH has been appointed director of the Atomic Energy Commission's Division of Controlled Thermonuclear Research to succeed Dr Roy W. Gould, who returned to the California Institute of Technology in August. Dr Hirsch was previously senior scientist in the division, which has a budget of about \$40 million in the present financial year. Dr Hirsch, 37, received his PhD from Illinois and has worked in industry on thermal and fast fission reactors, space nuclear propulsion and plasma physics.

Bowel Cancer

THE National Cancer Institute will award grants totalling \$2.50 million for 1973 for a research programme on the prevention, diagnosis and treatment of cancer of the large bowel. The grants will also include spending commitments for four more years of research. The programme is being directed by Dr Murray M. Copeland, professor of surgery at the M. D. Anderson Hospital and Tumor Institute, who is chairman of a group of working scientists who will solicit proposals from the scientific community, review them and make recommendations to the National Cancer Institute. Cancers of the rectum and large bowel are the second most common cause of cancer death in the United States.

Noise Control

THE Environmental Protection Agency has launched a major study of airport noise and is looking at the effects of establishing noise standards for trains and motor vehicles. The study will be the first action taken by the EPA under the powers given it by the Noise Control Act of 1972 (see *Nature*, 239, 483; 1972), which was signed by President Nixon late last month.

NEWS AND VIEWS

Gravitational Waves?

ON pages 136 and 140 of this issue of *Nature* there are two articles, by Sadeh *et al.* and by Mast *et al.*, on the question of the detection of gravitational waves with a seismometer. Sadeh *et al.*'s article has already stirred up a large amount of comment before publication and it is clearly high time that it sees the light of day in order that it can be evaluated by as many people as possible.

Sadeh *et al.*'s case is this. For a period of several months a digitizer was attached to a seismometer in Eilat, Israel. The seismometer was not the conventional narrow-band short period seismometer with a peak response around 1 cycle a second but of broader band, being responsive from 0.1 to 10 cycles a second. Broad band seismometers have not been widely used outside the Soviet Union because of the world-wide microseismic noise peak at 0.16 cycles a second, which is often a thousand times higher than the background noise at 1 or 2 cycles a second. This is less of a problem for digital recording provided the dynamic range is adequate, say 100 dB or more.

Digitized data were analysed in three and a half-hour sections by an autocorrelator and the singular peak shown in Fig. 1 obtained. This peak recurred on most, but not all days, after approximately 24 h. Evidence is presented that the phenomenon recurs at the period of the sidereal rather than the solar day.

Encouraged by this result to believe that they might be seeing gravitational radiation from a pulsar, Sadeh *et al.* sum the seismic signal in segments with time delays appropriate to the period of CP1133, a pulsar with a period close to twice that of the peak in the Fourier spectrum of Fig. 1 of the article. This yields two peaks (Fig. 6) separated by about 0.593. This value is half the optical period of CP1133 and is the expected period of gravitational radiation from the pulsar.

Sadeh draws the conclusion from these quite singular data that he is observing the rising each sidereal day of CP1133, whose gravitational waves excite the seismometer. There are problems of amplitude, to be sure. The expected signal according to Weber and Dyson is about eight orders of magnitude smaller than Sadeh's observation. The gravitational wave pundits, while accepting the uncertainty of their estimates, seem unwilling to move them up by this amount. Seismologists on the other hand would be unlikely to yield more than a gain of a factor of five as obtainable by favourable location of recording stations. Any suggestion that faults may isolate sites and excite standing vibrations is not tenable.

Several seismologists went rapidly into action when Sadeh's news broke—to my knowledge at least four groups with high quality seismic data started attempting to reproduce the result. One such attempt is reported on page 140 by Mast *et al.* Another was reported by D. H. Weichert (Ottawa) at a geophysical symposium in Banff a month or two ago. Neither reports anything other than failure to find CP1133. Three years ago Wiggins and Press also reported a pulsar signal search using a large array. That too was unsuccessful.

Mast *et al.* follow as closely as possible Sadeh's tech-

niques. The seismometer used is of the more common narrower band variety, but this should have no effect on the observations except to suppress the microseismic peak at 0.16 cycles a second. Signal averaging techniques, which in Sadeh's example showed peaks separated by 0.59 s, produce nothing that could not be attributed to noise. Mast *et al.* are therefore sceptical of Sadeh's result. They declare that it is incorrect to conclude that Sadeh's signal-average plot either verifies the detection of or accurately measures the period of a pulsar signal.

Can more be said at this stage? The score so far seems to be one success and three failures. Perhaps this is the way it will be and one ought to let evidence accumulate for some time. This, after all, is how many ideas and discoveries are evaluated—by being exposed to the atmosphere. In this case more comment is necessary. Gravitational waves are arousing keen interest and large investments both in time and money have been made in designing and operating detectors. If there is profit in using seismic data, of which a vast amount already exists, astronomers should be descending on geophysicists in droves. If not, the sooner the tide of astronomers is stemmed the better. One of the important features in this particular case is that the subject is interdisciplinary. Such investigations frequently pose problems of mutual understanding and finding the right person to answer one's questions. Thus in the following an attempt will be made to give a fairly blunt view of the issues involved as seen from a seismological point of view.

It is difficult to take exception to the article by Mast *et al.* They show the instrument response, use a well known instrument, quote absolute values for the ground displacements and perform all the tests on their data that could reasonably be expected. The same cannot be said of Sadeh *et al.*

The first problem encountered is that of knowing exactly what the data looked like. The more broad band response of the Eilat seismometer will make it receptive to microseisms of frequency 0.16 cycles a second. These signals would be expected to be moderately coherent over long periods and to have ground motions of up to at least 10^{-6} m—a factor of 10^5 larger than the signal Sadeh claims to be observing clearly. Whither have the microseisms gone? There is nothing singular about the site at Eilat—data from a conventional seismometer nearby show typical microseismic noise levels. None of the data processing techniques described would be capable of suppressing this noise. It remains a mystery, but one which could be cleared up by a display of just a short stretch of data before any processing. The signal ought to be clearly visible as a sine wave riding on the microseisms.

Another problem also stems from this failure to show raw data when it is claimed that the signal at the pulsar period has a sidereal day periodicity associated with it. The spectrum is shown, as is also a distribution of maxima (neither overwhelmingly convincing that a solar day period is not being observed). But the distribution of amplitudes of maxima as a function of time—the raw data—is not shown. It may be remarked that analysis

of seismic noise in the 1 cycle a second band frequently shows a daily character simply because the noise of human activity is greatest in the day—not because the Sun radiates anything which gets into the seismometer. Sadeh *et al.* display a strange coyness towards discussing the amplitude of their effect. The only time an amplitude is quoted it is related to an assumed noise level. The vertical scales of the figures are completely lacking in units. Amplitude seems entirely arbitrary. To my recollection the original publicity quoted 10^{-11} cm. Mast *et al.* aim their remarks at a quoted level of 10^{-10} cm. In Sadeh *et al.*'s article it is 2×10^{-9} cm.

The authors are aware that seismometers sometimes register other than desirable signals and they have carried out some tests to eliminate machinery and electronics. Other tests seem highly desirable. The site could be moved a few kilometres, for example, and a different recording mode could be tried. Or a conventional seismometer could replace the present one. If all these changes still reproduced the signal, then things would begin to look interesting. Weichert showed a peak (at a different period) just like Sadeh's, but was able to find drive wheels in his recorder running at exactly that period. A pure speculation is that the seismometer Sadeh used has a spurious resonance. More cannot be said until the obvious follow-up experiments have been carried out and the data are more clearly shown. Until then nothing can be regarded as proved.

A second article by Sadeh also appears on page 139 in which it is claimed that CP1133 may be detected in its rising by moonquake activity. The evidence for this can be seen and evaluated from his Fig. 1. It apparently is true that the moonquake peak in activity has slipped from perigee. The times of largest strain in the Moon are, however, a resultant of Earth and Sun tides, and the hypothesis that it is this that controls moonquakes is apparently still tenable. This hypothesis certainly seems reasonably competitive with the pulsar explanation. —From our Geophysics Correspondent.

Chromosome Pairing

ONE of the central problems in genetics is the mechanism by which homologous chromosomes become associated with one another before the exchange of segments between them. This pairing occurs at meiosis and is followed by separation of the homologous chromosomes into different nuclei. Besides its intrinsic interest, understanding of pairing is important in plant breeding because its failure means a loss of regular separation of the chromosomes and hence lowered fertility. Indeed, irregularity of chromosome pairing has been a major handicap for plant breeders. This has come about because many crop plants are polyploid, that is, with more than two sets of chromosomes.

Polyploids are believed to have usually arisen by hybridization between related diploid species followed by doubling of chromosome number to give an allotetraploid. Doubling may happen again following hybridization between the allotetraploid and another diploid species, so giving rise to an allohexaploid. Examples of allohexaploid crop plants are *Triticum aestivum* (wheat) and *Avena sativa* (oats). Hybrid polyploids of natural

origin, such as these, show regular chromosome pairing, but in those induced artificially by hybridization and colchicine treatment, the pairing is usually irregular.

The occurrence of polyploids of hybrid origin raises the question of the meaning of the term homologous when applied to chromosomes. Thus, *Triticum aestivum* has twenty-one pairs of chromosomes derived from three ancestral diploid species each with seven pairs. The twenty-one different chromosomes are denoted by 1–7 and *A*, *B* or *D*, respectively, according to their parentage, the corresponding chromosomes from the three species being given the same number. There is evidently considerable homology, that is, similarity of nucleotide sequence, between these corresponding chromosomes such as, for example, No. 3 of the *A* set and No. 3 of the *B* and the *D* sets. On the other hand, there will be much closer homology—indeed, virtually identity of nucleotide sequence because wheat is regularly self-pollinated—between the two 3*A* chromosomes, and similarly with 3*B* and 3*D*. To distinguish these differing degrees of similarity, the term homologous is used only in the strict sense, for example, for the two 3*A* chromosomes. The awkward term homoeologous is used to describe corresponding chromosomes derived from different species, for example, 3*A* and 3*B*. In what follows such chromosomes are described as counterparts.

A significant advance in understanding the forces involved in chromosome pairing was the discovery in 1958 by Riley and Chapman (*Nature*, **182**, 713) at the Cambridge Plant Breeding Institute that in *T. aestivum* lacking chromosome 5*B*, pairing of counterpart chromosomes took place, that is, 1*A* with 1*B*, 1*A* with 1*D*, 1*B* with 1*D*, 2*A* with 2*B*, and so on. In normal wheat the pairing is strictly homologous (1*A* with 1*A*, 1*B* with 1*B*, and so forth). Later studies by Professor Riley and his associates (for example, Wall, Riley and Gale, *Genet. Res.*, **18**, 329; 1971) have implicated a gene called *Ph* (for pairing homoeologous) in the longer arm of this chromosome. This gene suppresses pairing between counterpart chromosomes.

Another important advance was the discovery earlier this year by Evans and Macefield (*Nature New Biology*, **236**, 110; 1972) in Professor Rees's department at the Institute of Rural Science, University College of Wales, Aberystwyth, that the presence of supernumerary or *B* chromosomes suppresses counterpart pairing in both diploid and tetraploid rye grass hybrids (*Lolium temulentum* × *L. perenne*). Supernumerary chromosomes are smaller than the normal ones and, unlike them, are dispensable.

In this issue of *Nature* (page 159), Dover and Rileý show that the effect of supernumerary chromosomes in *Triticum* is similar to that in *Lolium*, and can compensate for the absence of gene *Ph*. In other words, in the absence of chromosome 5*B*, supernumerary chromosomes suppress counterpart pairing. The importance of this discovery is two-fold. First, it suggests that gene *Ph* may have been derived in evolution from a supernumerary chromosome. This conclusion, if confirmed, would add significantly to understanding of the function of these chromosomes. Second, from the point of view of plant breeding it may be possible, as Evans and Macefield suggested, to use supernumerary chromosomes to achieve regularity of chromosome behaviour at meiosis, and hence high fertility, in synthetic allopolyploids. It is

now evident that incorporation of part of a supernumerary chromosome into an ordinary chromosome might achieve the same result.

Dover and Riley have made a further discovery concerning chromosome pairing in *Triticum* and its allies. The supernumerary chromosomes whose effect they studied were derived from *Aegilops mutica* and *Ae. speltoides*, which are grasses closely allied to wheat and able to hybridize with it. Recently, Dover and Riley (*Nature New Biology*, **235**, 61; 1972) found that hybrids between *T. aestivum* and different individuals of the cross-fertilizing species *Ae. mutica* could be grouped into four classes as regards their pairing behaviour and chiasma frequency. It seems that individual plants of *Ae. mutica* are often heterozygous at one or both of two independently inherited gene loci affecting the pairing of counterpart chromosomes. Dover and Riley have now studied the relationship between the action of these genes and the other factors known to affect counterpart pairing, namely, gene *Ph*, and supernumerary chromosomes. This investigation involved crossing individual plants of *Ae. mutica* and *T. aestivum* of appropriate genotypes and recording chiasma frequencies.

The authors found that all *Ae. mutica* genotypes behaved alike in hybrids with wheat lacking chromosome 5B, giving a low frequency of counterpart pairing if supernumerary chromosomes were present and a high frequency in their absence. Thus, the genetic variability within *Ae. mutica* in the degree of counterpart pairing seems to arise through modification of the effect of *Ph* rather than through a primary effect. In support of this idea, it was found that counterpart pairing, and hence chiasma frequency, was greater in the absence of chromosome 5B than with even the most extreme *Ae. mutica* genotype in the presence of 5B, suggesting that no *Ae. mutica* genotype completely inactivates *Ph*.

Nothing is known about the mechanism of chromosome pairing at the molecular level, but Watson and Crick (*Nature*, **171**, 964; 1953) suggested that it involved the pairing of complementary nucleotide chains to form a double helix. There seems to be no alternative to this to account for the specificity of pairing, and a more detailed hypothesis along these

lines has recently been proposed by Sobell (*Proc. US Nat. Acad. Sci.*, **69**, 2483; 1972). On the other hand, the suppression of pairing between counterpart chromosomes in *Triticum* brought about either by gene *Ph* or by supernumerary chromosomes, and the partial relaxation of this suppression by *Ae. mutica* genes, cannot result from changes in nucleotide sequence, but must involve action at a different level of organization. Electron microscopy at the pachytene stage of meiosis has revealed a protein framework about 150 nm wide called the synaptonemal complex lying between the two chromosomes of each pair and extending their whole length. The synaptonemal complex of each bivalent is attached to the nuclear membrane at both ends but not in intervening regions. This was first demonstrated by Woollam, Ford and Millen (*Exp. Cell Res.* **42**, 657; 1966) with several mammals.

A plausible hypothesis, therefore, for the mode of action of genetic factors influencing counterpart pairing is that they alter the relative positions on the nuclear membrane of the sites to which the ends of homologues and of their counterparts become attached. Sved (*Genetics*, **53**, 747; 1966), Feldman (*Proc. US Nat. Acad. Sci.*, **55**, 1447; 1966) and Riley (*Genetica Agraria*, **21**, 111; 1967) have already favoured such an explanation on other grounds.

H. L. K. W.

PROTEINS

Egregious Enzymes

from our Molecular Biology Correspondent
MANY monstrous and horrid shapes are now to be found in the Enzyme Catalogue, to the point that generalizations concerning permitted symmetry modes have come to appear increasingly futile. Two extraordinary new additions to the bestiary have now been transfixed by the electron microscopist's art, and deserve a leisurely inspection.

Louie *et al.* (*J. Mol. Biol.*, **70**, 651; 1972) have looked at an enzyme from *Pseudomonas*, pyridine nucleotide transhydrogenase, which catalyses the reduction of NAD by NADPH. The reverse reaction is not favoured, except in the presence of an activator, 2'-adenylic acid. Now this activator, by several criteria, provokes far-reaching structural changes in the enzyme: there is an immunologically manifested change, detected by the extent of complement fixation; there is a large enhancement of the fluorescence from

the FAD, which is present in the molecule, and the polarization of this emission is also increased, which is interpreted in terms of a decrease in cofactor mobility; and in particular, the sedimentation coefficient decreases dramatically.

To show that this effect—clearly a dissociation—is related to the enzymatic activation by the 2'-AMP, scanner optics were used to observe the sedimentation in the concentration range of activity assays; indeed the progress of the active species could be followed by the absorption change in zone sedimentation through a substrate solution. In the absence of the activator the sedimentation coefficient is 110S, corresponding to a very large aggregate, and in its presence it falls to 28S. Electron microscopy shows what happens: the unactivated enzyme appears as long filaments of variable length, mostly 200–500 Å, but sometimes as much as 5000 Å. The fine structure in these molecules looks rather like a screw thread running along the filament, with a pitch of 100–200 Å. When 2'-AMP is added to the enzyme, the filaments vanish, and give place to stubby particles, circular in one projection, and square in the other. There seems to be a ring of particles disposed around a hollow core, and striations in the side projection suggest that there are four rings of subunits. From the size of the particles and the content of FAD per unit mass of protein, Louie *et al.* suggest that they may contain something like twenty chains, each of about 40,000 molecular weight.

The existence of enzymes in highly associated filamentous forms is of course nothing new; glutamate dehydrogenase is a familiar example. In the transhydrogenase, however, the aggregation is associated with a conformational alteration, and a change of functional emphasis, from the reverse to the forward reaction. The homogeneous form may well be a tight helix, which in the absence of the activator untwists somewhat, and in this form aggregates to large filaments—a situation not unlike the association of TMV protein, where the binding or release of protons causes a rather similar transition between a planar disk and a dislocated, helical form, which alone has the capacity to polymerize.

A stranger beast is the Mickey Mouse enzyme (the authors' description), transcarboxylase, which has been studied by Green *et al.* (*J. Biol. Chem.*, **247**, 6284; 1972). This is a complex structure, which in its native form sediments at 18S, with a molecular weight of 790,000. It rather readily sheds three successive 6S subunits, each of 144,000 molecular weight, the sedimentation coefficient decreasing by 2S at each stage in the process. The

residual 12S core, with a molecular weight of 360,000, dissociates further under progressively more severe conditions to three subunits of 120,000, and finally to six of 60,000. The 6S fragments that are initially shed are shown in the accompanying paper (Ahmad *et al.*, *ibid.*, 6299) to contain both the biotin cofactor which is implicated in the carboxyl carrier function, and the divalent metal (a mixture of zinc and cobalt). The biotin and the metal ions are in separate subunits of the 6S protein, the former on 1.3S chains of 12,000, the latter in 2.5S chains of 60,000 molecular weight, of which there are six.

Electron microscopy reveals that the 12S particles are circular, with a hole in the middle, or rectangular from the side, whereas in the intact native 18S enzyme the circular core bears three smaller attached objects on its periphery, not in general symmetrically disposed. These bodies are the 6S subunits, and when one of them dissociates, as it does under mild conditions, the residual molecule looks like a head with two ears, that is to say a Mickey Mouse. The unusual symmetry of the system becomes even odder on closer examination. The central "head" consists of three square subunits arranged round a three-fold axis, each evidently containing two of the basic 60,000 chains. A curious feature is that the ears are not symmetrically disposed in relation to either the three-fold axis or the transverse plane of symmetry, but are attached to one edge of the disk, like feet. The generally asymmetric and rather variable disposition relative to the three-fold axis is interpreted to indicate a flexible inter-chain bond, rather like that seen in antibodies. The position of the biotin can be established by labelling it with avidin, which being avid for biotin, binds wherever the cofactor is accessible. The attachment sites are arranged symmetrically, and are located at the junctions of the head with the ears.

It thus seems that the carboxyl carrier chains extend from the head along the ears, but that by virtue of the flexible connection the ears can waggle about this axis. The intact enzyme can be reassembled from separated heads and ears. When the conditions of dissociation and reassociation are changed, however, a singular phenomenon is observed: a new species, enzymatically active and sedimenting at 24S, is generated, which is seen in the electron microscope to have two sets of ears, three on either side of the central disk plane. This new-found dihedral symmetry indicates the presence of a set of binding sites, made manifest after a slight change in solvent conditions, which may arise from gene duplication. Altogether a weird specimen.

ORNITHOLOGY

Safety in Numbers

from our Animal Behaviour Correspondent
WHY do many birds move around in flocks instead of singly? The advantages to be gained from being part of a group are usually thought of as being either protection from predators or ease of finding food. It is fairly easy to see why clustering together could help birds to combat their predators: more pairs of eyes will be better able to detect danger in the first place and mobbing or mass attacks may successfully drive away a predator, for example. It is less obvious why it should be easier for a bird to find food in a group than on its own.

Krebs *et al.* (*Ibis*, 114, 507; 1972) have recently demonstrated that one reason why a single bird may be at a disadvantage when seeking food is that it is unable to exploit finds of food made by its flock mates. Using captive great tits, they showed that the members of a flock "copy" one another. If one bird finds food, the others will find it as well, as a result of searching in the same area. It was found that all the members of the flock would immediately concentrate their search in the place where food had been discovered by one of them.

The exact location of food was, however, not the only thing which the birds could learn from their flock mates. In one experiment, four different types of food container were dispersed throughout the test area. Once one bird had found food in one type of container, the others would search specifically in

that type. An interesting finding was that the degree to which the birds copied one another was dependent on the kind of food distribution they had experienced previously. If they had been used to finding a lot of food in one place, they would copy to a greater extent than if they were used to hunting for small pieces of food dispersed over a wider area. It is clearly more worthwhile for a bird to copy another if that bird has found a large amount of food rather than a single food item.

Although there are, of course, many differences between captive groups and flocks in the wild, these experiments do strongly suggest that flocking of great tits can be of benefit to the participants because it increases their effectiveness in finding food.

SOIL

Nutrient Losses

from a Correspondent

LAND drainage is a potential source of pollution of surface and underground water supplies, and because most of the elements involved are plant nutrients it also causes a financial loss to the farming community. The leaching/drainage process was discussed in London on October 17 at a symposium organized by the Agriculture Group of the Society of Chemical Industry; attempts were made to quantify and predict the losses which occur.

Mr P. H. Nye (University of Oxford) has found that although soil acts as a chromatographic column, any simple predictive approach fails because of the practical complexities of variation in

Satellite DNA and Speciation

THE function and evolutionary significance of satellite DNA—DNA which has a reiterated base sequence, is associated with heterochromatin and centromeres and may or may not be transcribed—remain tantalizing mysteries. It seems unlikely that these simple sequences code for any polypeptide and it has, therefore, been suggested that satellite DNA may be involved in processes such as pairing of homologous chromosomes, chromosome movement and chromosome packing, but there is little evidence in support of these speculations. Mazrimas and Hatch, who, as they report in *Nature New Biology* next week (November 22), have compared the amounts of satellite DNA in the genomes of twelve of the twenty-two species of kangaroo rats of the genus *Dipodomys*, now suggest that satellite DNA may facilitate the reassortment of genes by recombination and thereby promote genetic flexibility.

Their argument is based on their ob-

servations, first, that among the species of *Dipodomys* the amount of satellite DNA is more or less inversely correlated with the degree of evolutionary specialization and, second, that the amount of satellite DNA is positively correlated with the number of subspecies of each species. Furthermore, the amount of satellite DNA is positively correlated with the sum of the number of arms of all autosomal chromosomes but is not correlated with protein polymorphism.

It seems therefore that in this genus unspecialized species with a broad geographical distribution have more satellite DNA than species specialized to occupy narrow ecological niches. Survival of a species over a broad geographical range and in a variety of ecosystems is believed to depend on a high genetic flexibility conferred by genetic recombination and Mazrimas and Hatch suggest that satellite DNA may be involved in supragenetic functions including recombination.

soil properties down the profile, intermittent movement of water, interaction between the soil and the nutrients and so forth. Any model of leaching must deal both with water movement through the soil and with the interaction of the nutrients that it carries with the soil: at present there is insufficient knowledge to allow a model to be built up on a purely theoretical basis. The attempt to formulate theoretical models does, however, have the added advantage of guiding research into the most fruitful areas.

An alternative approach is to use numerical computer solutions to find the parameters necessary in the predictive equations. This approach can be used where a sufficient body of practical data exists for a particular situation. Much more information is needed to extend such models to the more general cases and the remaining speakers provided instances of how this information has been collected in practice. Information on both water and salt movement through soil was provided by lysimeter studies discussed by Mr A. J. Low (ICI, Jealott's Hill), Mr E. A. Garwood (Grassland Research Institute, Hurley) and by Mr J. Webber (ADAS, Leeds). Relevant information can also come from measurements of nutrient losses from agricultural topsoils as was reported by Mr R. J. B. Williams and Dr J. Bolton (Rothamsted Experimental Station).

The lysimeter studies emphasize that water movement through the profile is related to crop growth. Transpiration by a healthy crop much reduces the amount of water that is available for leaching. The situation is more complex, however, in that, for example, clover delays the onset of leaching longer than a grass canopy although the amount of water transpired is less. The Hurley workers have found another complexity of the water/crop interaction. Here nutrient loss in winter was related to the amount of water that had been available to the crop during the previous growing season. This was because drought restricted nutrient uptake (particularly nitrate) and so left greater residues in the soil for leaching during the following winter.

Nutrient losses from the topsoil of the Rothamsted experimental field Broadbalk during the past 100 years were presented. Here, a knowledge of the relationships between ions in the soil solution (primarily dictated by pH and CO₂ partial pressure) allows detailed information on calcium loss to be used to predict total nutrient losses.

Perhaps the most practical suggestion which emerged from the meeting was from Mr Williams who suggested that losses of nitrate from the topsoil would be minimized if soil could be engineered to store more water and hence more nutrients within the rooting zone.

FRESHWATER FISH

Irish Studies on Gudgeon

from a Correspondent

A RECENT study by Michael Kennedy and Patrick Fitzmaurice on some aspects of the biology of the gudgeon in Irish waters (*J. Fish Biol.*, 4, 425; 1972) has made an important contribution to the body of knowledge about the life history of this fish. The gudgeon is a small bottom-living member of the carp family which is widely distributed in Europe. Partly because of its size (it rarely grows to a length greater than 20 cm) it is not the subject of great interest to inland fisheries, and few attempts have previously been made to study its life history or its relations with more economically important fishes.

The gudgeon is not a native fish in Ireland, having been introduced at some unrecorded date, and its distribution, although not well known, seems to be patchy. It is known to be common in the catchments of the Erne, the Boyne, the Cork Blackwater, the Lee and the Shannon, although it occurs in small numbers elsewhere, including still waters. Kennedy and Fitzmaurice studied samples from several reservoirs, lakes and streams, including trout streams in Co. Cork, and from the Grand Canal in Co. Dublin.

This is the first study to have been made of Irish gudgeon and the authors find general agreement between the life style of the species that is published

in studies of European and British gudgeon, although one of the most important, B. Bernet's work (*Ann. Sta. Cent. Hydrobiol. Appl.*, 8, 129; 1960), is not mentioned.

The preferred habitat of the gudgeon seems to be gravel-bottomed rivers and streams, although when reservoirs were constructed on the River Lee, a great increase in the gudgeon population was observed for a short period, followed by a return to a more normal density. Its food varies considerably with its habitat; young gudgeon in still waters feed on Cladocera and copepods to a much greater extent than those living in rivers. No matter what the environment, the principal foods eaten by the gudgeon are chironomid and trichopteran larvae, and ephemeropteran nymphs. In some localities large numbers of molluscs are eaten, in others filamentous algae are consumed. In general terms the gudgeon in Ireland is an adaptable fish feeding on, or close to, the bottom on whatever invertebrates are locally abundant, and even capable of utilizing algae as food (possibly in the absence of adequate animal prey).

Although the gudgeon is not regarded as a noticeable fish for inland fisheries purposes its potential as prey for, and competitor with, more valuable fishes has to be assessed. It is this aspect which clearly interests the staff of the Inland Fisheries Trust, and which has led to a series of valuable studies of the

Vesicular Stomatitis Virus Pseudotypes

IN next Wednesday's *Nature New Biology* (November 22) Zavada and his colleagues describe a new and ingenious technique they have developed to search for putative human cancer viruses. Zavada has found that when vesicular stomatitis virus (VSV), an enveloped RNA virus which is not oncogenic, infects chick cells previously infected by the oncogenic virus avian myeloblastosis virus (AMV) some of the progeny particles released are pseudotypes—VSV genomes enclosed in an envelope which has AMV antigens. These pseudotypes can be neutralized by anti-AMV antisera but not by anti-VSV antisera and they have the host range and interference specificities of AMV, not VSV.

When wild-type VSV is used to infect cells already infected with AMV some wild-type VSV particles are produced in addition to VSV(AMV) pseudotypes. To eliminate these contaminating wild-type VSV particles Zavada selected mutant strains of VSV the virus particles of which are more thermolabile than the wild-type particles. He then infected with these mutant VSV cells infected with AMV and simply by heat-

ing eliminated progeny VSV particles enclosed in VSV envelopes. The pseudotypes, VSV genomes in AMV envelopes, survived because the temperature sensitive lesion in the mutant VSV strains is located in a component of the VSV envelope.

Zavada and his colleagues have, as they explain in their second report, infected cultures of human mammary carcinoma cells, HeLa cells and other human cells with such mutant VSV and screened for progeny particles which are not thermolabile and lack VSV neutralization antigens. Only the human mammary carcinoma cells yielded such particles and the possibility remains that these particles are pseudotypes with VSV genomes in envelopes the antigens of which are specified by a putative human tumour virus resident in the mammary carcinoma cells.

Of course this is not the only possible explanation of the origin of these VSV pseudotypes but it has not yet been excluded and the method seems to provide a new approach to the problem of screening human cancer cells for traces of human cancer viruses.

biology of freshwater fishes in Ireland, of which this is the latest.

Kennedy and Fitzmaurice report that gudgeon occur commonly in the stomachs of pike in the Lee and Blackwater systems, and that trout in the former river also eat them. In one of the newly built Lee reservoirs the gudgeon population greatly expanded between 1959 and 1963, and between 40 and 80 per cent of the trout in the reservoir were eating them. This figure has fallen to almost zero since the gudgeon population declined.

This study thus shows that the gudgeon has some importance as a food fish for trout, and to a lesser extent for pike. The authors, however, make no comment on any competition that it may offer to the former species, a far more valuable fish. Young trout in small streams eat substantially the same groups of invertebrates as does the gudgeon, and therefore there may well be a considerable degree of competition.

PESTICIDES

Resistance in Arthropods

from a Correspondent

AN important aspect of the battle against hunger and suffering, especially in the developing countries, is the control of arthropod pests that attack food before or after harvest or are vectors of debilitating diseases. When few chemicals are available to control a particular pest the development of strains resistant to one or more of these compounds can have serious consequences. Scientists involved in pest control are conscious of the dangers and at a meeting in London of the Pesticides Group of the Society of Chemical Industry on October 16 they took stock of the situation and discussed future prospects.

Professor J. R. Busvine (London School of Hygiene and Tropical Medicine) reviewed the progress made during the past 25 years. Methods that are simple, reliable and reproducible under adverse conditions in the field have been developed to assay a pest for resistance. Laboratory studies can then establish the range of pesticides that the pest can tolerate—it is alarming that an insect strain can develop resistance not only to the compound to which it was subjected but also cross-resistance to chemically unrelated structures it has never encountered. The pick-up, metabolism (activation or detoxication) and excretion of the insecticide in resistant and susceptible strains are investigated. Frequently lack of control in the field occurs when several mechanisms reinforce each other and they may be

differentiated by genetic studies on the resistant strains.

The closed environment of a glasshouse is ideally suited to the build-up of resistance. In commercial glasshouses in the United Kingdom strains of the aphid *Myzus persicae*, red spider mite, leaf miners and whitefly occur that are resistant to many pesticides. Frequency of harvesting further limits the choice of compounds. Dr N. W. Hussey (Glasshouse Crops Research Institute) stated that he and his colleagues aim to prolong the commercial life of pesticides by integrating their use with biological control measures. The effect of pesticides and fungicides on the beneficial species must be considered and, ironically, two of the systemic fungicides more satisfactory on this score have potential problems with the arrival of strains of tolerant fungi.

Another aspect with specific problems is the control of cattle ticks. Mr E. C. Wilmshurst (Thurgarton Research Station) stressed that the methods of pesticide application normally used—driving the cattle through dips or sprays—are unsatisfactory because the dose a beast receives cannot be accurately controlled. Tolerance was first encountered to sodium arsenate but in the past 20 years cases of resistance and cross-resistance to chlorinated hydrocarbons, carbamates and organophosphates have been reported. Though resistance to a given compound can develop in several continents over a period of about two years the outbreaks are independent and localized. A new method of application is required; a “pour-on” technique with 100 millilitres per beast of an experimental compound, which is systemic in cattle, shows promise.

Mr C. E. Dye (Pest Infestation Control Laboratory) stated that surveys of insects of stored products indicate that eleven species of Coleoptera and five of Lepidoptera show resistance to

at least one group of insecticides. Genetic studies have not been made to provide the crucial evidence but observations on the effect of synergists, the relationship between tolerance and chemical structure and metabolic studies in susceptible and resistant strains, show there are several mechanisms involved. Metabolic factors are implicated and may account for the resistance of a strain of *Tribolium confusum* to synthetic analogues of a juvenile hormone and to several other types of insecticides.

Professor Busvine had stressed the need for collaboration between zoologists, geneticists and biochemists. An excellent example of such cooperation is provided by scientists at Rothamsted Experimental Station, three of whom summarized their recent work. Dr R. M. Sawicki, using genetic markers, has isolated strains of *M. domestica*, showing single resistance factors, the mechanisms of which could be established, and re-linked them by crossbreeding. Flies which showed resistance to organochlorine, organophosphorus and carbamate insecticides revealed the wide range of mechanisms that may operate. Mr A. W. Farnham reported similar studies on *M. domestica* resistant to natural pyrethrum extract (strain NPR) or to resmethrin (strain 104), a synthetic pyrethrin. These strains were selected in the laboratory—most cases in the field of resistance to the pyrethrins have occurred as cross-resistance when other types of insecticide had been used. Dr A. H. Devonshire discussed the results of his biochemical studies on resistance in *M. domestica* and *M. persicae*. The co-factor requirements and substrate specificities of enzymes isolated from strains susceptible or resistant to various insecticides help to differentiate the mechanisms involved. He noted the role of oxidases in activation or detoxication of various pesticides. These

Mica Sheets and Molecular Interactions

In next Monday's *Nature Physical Science* (November 20) Bailey and Daniels describe an elegant experiment by means of which they have measured some of the parameters defining the force of attraction between two pieces of mica in close proximity.

The essence of their device is a pair of narrow strips of mica, each some 5 μm thick, which touch each other near one end and are held apart at the other. Bailey and Daniels measured the precise separation profile of this delicate arrangement by multiple beam interferometry.

Theoretically the attraction between the two pieces of mica can be expressed in terms of calculable parameters like

the Madelung constant and the number of ion pairs per unit area. The total force is, of course, made up of ionic and dispersion forces, the former of which contribute about ten times as much to the overall surface energy as the latter. Other parameters in the expression for the attraction were then altered until the calculated effect on two (non-interacting) sheets was as close as possible to the effect of real forces.

Bailey and Daniels particularly draw attention to the fact that one of the “best-fit” parameters, the so-called equilibrium contact separation, turns out to be 7 nm which is almost exactly the thickness of two monomolecular layers of water molecules.

three speakers stressed the dramatic effect when two or more mechanisms, each quite modest alone and difficult to quantify, are combined in a given strain. The concentration of the toxic entity at the target site is the criterion for death. The marked reinforcement of individual mechanisms—for example, a combination of slower penetration to the target site—increased storage in non-vital organs and increased detoxication, can then be understood.

HELIUM

A New Superfluid?

from a Correspondent

It seems likely that a new superfluid phase with rather bizarre properties has been discovered in ^3He by Osheroff, Gully, Richardson and Lee (*Phys. Rev. Lett.*, **29**, 1920; 1972). They have further studied the thermal anomalies they previously found to occur at the very low temperatures reached in a Pomeranchuk compression cell (of the order of 2 to 2.5 mK) (*Phys. Rev. Lett.*, **28**, 885; 1972). Originally these anomalies were ascribed to an anti-ferromagnetic transition in the solid, long expected near this temperature, but the new measurements, which are very detailed and ingenious studies by nuclear resonance techniques, seem to show convincingly that both are phase transitions occurring in the liquid; transition A is a second-order transition near 2.7 mK, and the second, B, is at a temperature about 20 to 30 per cent lower and of first order. The result will cause considerable excitement among many-body theorists.

Speculations on such a phase, the "anisotropic BCS superfluid", were begun a dozen years ago by Brueckner, Soda, Anderson and Morel (*Phys. Rev.*, **118**, 1442; 1960) and independently, but later, by Emery and Sessler (*Phys. Rev.*, **119**, 43; 1960). The properties have also been discussed by Anderson and Morel (*Phys. Rev.*, **123**, 1911; 1961) and by Balian and Werthamer (*Phys. Rev.*, **131**, 1553; 1963).

^3He at these temperatures is known to be a true "Fermi liquid": the atoms, which have a nuclear spin I of $\frac{1}{2}$ and obey Fermi statistics, are best described as occupying states in a Fermi sea, just as do the electrons in a metal. Thermal, magnetic, and transport measurements all verify that there is a Fermi surface and that the spectrum of excitations consists principally of single "quasi-particle" and "quasi-hole" states near the Fermi surface. The Fermi energy corresponds to a temperature of about 0.5 K, so at temperatures of a few mK the liquid is highly condensed—for instance, the nuclear spin susceptibility is only about a hundredth of the susceptibility of the solid at the corresponding temperature. The entropy of

this condensed state is lower than that of the solid, in which the spins are relatively free, and this is why adiabatic compression, by converting liquid into solid, is a cooling mechanism.

It was natural to ask whether this Fermi system would also undergo a BCS transition to a superconducting state, as does the electron gas in most metals. The answer is apparently that ^3He cannot exhibit the standard BCS transition, but can undergo a new type, in which the condensed pairs are in states of non-zero total spin and orbital angular momentum: possibly $L=1$, $S=1$; $L=2$, $S=0$; or $L=3$, $S=1$. Because all condensed pairs must go into the same state the result may be a state of finite total angular momentum with peculiar spatial anisotropies, surface properties and so on. (As the atoms are neutral, the phase must be a superfluid and not a superconductor.) In particular, as Leggett (to be published) and independently Anderson and Varma (*Nature*, in the press) have recently shown, one of the striking results of Osheroff *et al.*, a large shift of the nuclear resonance frequency between the A and B transitions, is a property of some anisotropic Anderson-Morel superfluids.

Although no valid quantitative prediction of the critical temperature T_c has been made—estimates range from 10^{-7} to 0.07 K—the fact that it is far below the Fermi temperature argues strongly for a BCS transition, as does the second-order nature of the phase transition. But so far not one of the remarkable variety of Anderson-Morel states has been shown to agree with all the experimental facts: rather, each

new observation suggests a different state. Finally, of course, there is as yet no experimental evidence for superfluidity, which would be the crucial test of the theoretical speculations.

DISPLAYS

Odds on Plasma Panels

from a Correspondent

It was appropriate that the physics of display devices should be the subject of a meeting organized by the Institute of Physics at Imperial College, London, on October 25, for electronic devices are becoming steadily more commonplace in industrial, military and domestic applications, and it has become necessary to develop more sophisticated means of displaying the information they produce. Display devices now being developed include electroluminescent diodes and panels, plasma panels, liquid crystals and various displays employing incandescent tungsten filaments.

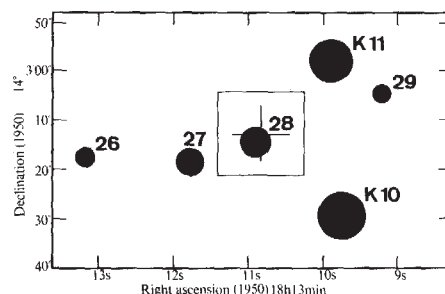
Most displays take one of two forms, either a "7-bar" arrangement (two rhombi with a common side), used primarily for the display of numerals, or a 7×5 matrix of dots for alphanumeric information—letters, numbers and other symbols. The distinction is important, for the modes of address are quite different. All the elements of a bar display may be addressed in parallel using standard decoders available in integrated circuit form. For a matrix display, however, it is generally preferable to adopt a scanning mode of address in which only the dots of one particular row are driven at any given

Identification of GX 17 +2

UNTIL more orbiting X-ray telescopes with the pointing accuracy of Copernicus become available, the optical identification of counterparts to X-ray sources must remain a painstakingly laborious process. One of the best ways to obtain a reasonable idea of exactly where such sources might lie is to find a radio counterpart, and then search the radio error box, which is usually smaller than the equivalent X-ray error box. This is just what Reina and Tareghi, of the University of Milan, have done in the case of GX 17 +2, and they present the fruits of their labours in next Monday's *Nature Physical Science* (November 20). For this source, only one optical candidate is visible on the Palomar Sky Survey plates within 3σ of the radio position given by Hjellming and Wade (*Astrophys. J. Lett.*, **168**, L21; 1971).

There is one snag, however. If GX 17 +2 is like Sco X-1, which is the only standard by which such sources can be judged, then the optical counter-

part would be 24 mag, and too faint to appear on the survey plates. Certainly, star 28 in the diagram would appear in the error box by chance with a probability of about 0.5; a rather more interesting possibility is that the X-ray source might be an optically invisible binary companion to star 28, which might then be a type B star with apparent magnitude 18 at a distance of just under 55 kpc. Perhaps this source now qualifies as one of the more interesting objects, which will receive priority on the Copernicus viewing schedule.



time. Any given element is thus driven for only $1/n$ of a cycle (for a display of n rows) and the brightness is correspondingly lower unless the drive is n times greater or unless some form of memory is either provided or is inherent in the device. If the mechanism of the display is one which saturates at high levels of drive, then the former alternative does not exist. Much of the discussion at the meeting consequently centred on questions of memory, saturation and drive mechanisms.

Nematic liquid crystals were shown by Dr C. J. Gerritsma (Philips Research Laboratories, Eindhoven) to hold considerable promise for many display applications. The "twisted nematic" display in which a helical arrangement of molecules is disrupted by the application of a potential difference can be operated at voltages directly compatible with integrated circuits. The mode of operation which has so far been more widely exploited, however, is "dynamic scattering" in which the liquid crystal changes from a clear to an opaque state when a voltage is applied. The requires rather larger drive voltages (10–20 V).

The various modes of operation exhibit thresholds with varying degrees of sharpness, that for dynamic scattering being the least sharp. A consequence of this is that when the scanning mode of address is adopted for matrix displays (with half the drive voltage applied to the row and half to the column electrodes) many of the elements not being driven experience half the drive voltage and scatter appreciably, thereby weakening the contrast. Dr C. Gooch (Services Electronics Research Laboratory, Baldock) described techniques for markedly improving the contrast of displays based on the dynamic scattering of liquid crystal by applying additional voltages to the unselected rows and columns.

Liquid crystal displays saturate large drive voltages, but their relatively long decay time (~ 100 ms) compared with their rise time (10 ms for dynamic scattering) was said by Dr Gooch to be sufficient for a scanned display of about ten lines without additional memory.

Gas discharge devices, which were surveyed by Mr G. Weston (Mullard Research Laboratories) do not show saturation effects, and matrices of discharge cells ("plasma panels") can be operated in the scanning mode either by the application of greater drive voltages or by using a sustaining voltage to produce a memory effect. They can fairly readily be produced in large areas with up to 60 lines an inch, have high brightness, are compact and with the addition of phosphorus can give multi-coloured displays, and it was suggested that perhaps plasma panels offer the best, although still distant, prospect of a replacement for the cathode ray tube.

CREEP

Steel and High Temperature Alloys

from a Correspondent

THE recent conference on creep organized by the Iron and Steel Institute and held in the University of Sheffield between September 20 and 22 was particularly successful in bringing together metallurgists working on the basic strengthening mechanisms of steels that are resistant to creep and those concerned with the problem of obtaining data on creep for design purposes.

The first session was concerned with the basic concepts of creep strength and included contributions from Professor R. Lagneborg (Royal Institute of Technology, Stockholm) who introduced a dislocation model of creep, and Dr C. M. Sellers (University of Sheffield) who presented a review of the structural changes that can occur in two-phase alloys during deformation at high temperature. Dr B. Wilshire (University College, Swansea) spoke about his ideas on internal and effective stress, and this particular topic was referred to frequently in the course of the meeting.

A contribution from Mr R. F. Johnson and Dr J. Glen (British Steel Corporation) introduced the second session during which some of the engineering aspects of creep were considered. These authors were critical of the value of some of the research that has been carried out on creep mechanisms, for the work has contributed little to the basic purpose of creep testing, namely the supply of design data to engineers. They pointed out that design data are now being required for times up to 250,000 h and conventional extrapolation techniques could scarcely be expected to supply this information, especially for new steels where few data exist. Consequently they asked that efforts be directed towards obtaining fundamental information that would be helpful in deriving design data valid for long durances. These remarks, not unexpectedly, provoked considerable comment, and it was suggested that some recent theoretical work provided relationships that could be used for long-time prediction. The general impression, however, was that there is a lack of communication between those concerned with the physical metallurgy of creep and those whose task it is to supply reliable creep information for design purposes. Perhaps, as a consequence of the discussions at this conference, the two groups will be encouraged to work more closely.

The microstructure and creep of austenitic steels and Ni-base alloys was the topic for the third session, and several contributors described work

being carried out on 25 per cent Cr and 25 per cent Ni austenitic steels stabilized with Nb, particularly with regard to the metallography of the precipitation of NbC. A contribution by Professor B. Aronsson (Swedish Institute for Metal Research, Stockholm) emphasized the importance of small amounts of nitrogen in improving the creep strength of type 316 austenitic steel; it was suggested that the improvement is due to nitrogen in solid solution rather than to precipitation of nitrides. In a particularly interesting paper, somewhat away from the principal theme of the session, Mr E. G. Wilson (UKAEA, Springfield) described creep experiments on 20 per cent Cr and 25 per cent Ni austenitic steel containing Nb in which the stress was varied. He emphasized the significance of anelastic creep in explaining some of the observations.

The importance of recovery in controlling creep behaviour was clearly demonstrated in a paper by Mr B. E. Hopkins and Dr T. B. Gibbons (National Physical Laboratory) describing creep experiments in Ni-base alloys. They also put forward the interesting suggestion that the dependence on grain size of the minimum creep rate observed in these alloys could be explained if recovery is somehow easier adjacent to grain boundaries.

The final session dealt with the microstructure and creep of ferritic steels and was dominated by papers by Dr J. D. Baird and his co-authors (General Steels Division of the British Steel Corporation). They have made a thorough and exhaustive study of the factors controlling the creep strength of iron alloys. In particular they have shown that interactions in solid solution (between Mo and C and N for example) can be important in short-time creep tests at 550° C, but after about 1,000 h precipitation becomes important and solid solution effects less significant. The importance of dislocations in refining intragranular precipitation was emphasized, and the suggestion was made that the optimum density of dislocations may be achieved in upper bainite.

It would be reasonable to conclude, on the basis of the evidence presented at this meeting, that knowledge of the principles of strengthening for creep resistance has progressed to the stage at which suitable alloys can be specified with some confidence. When the difficulty of providing creep data for the design of components for service at high temperature is considered, however, the situation is less satisfactory, but rapid progress towards a solution can be anticipated.

Hypersonic Flight

J. L. STOLLERY

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This article discusses the problems of hypersonic flight and describes the relevant research at Imperial College with particular reference to the design of space shuttles.

HYPERSONIC flight can conveniently be defined as flight at a Mach number, M , greater than five. As such high speed flight is likely to occur at high altitude the hypersonic flow regime covers a very wide spectrum of flow conditions ranging from the near vacuum of outer space through free molecule, transitional and finally the continuum flow conditions in which all conventional aircraft fly. In the continuum flow regime the local temperatures generated near the body by shock compression and skin friction are so high that air no longer behaves as a perfect gas. Vibration, dissociation, electronic excitation and finally ionization can occur, and a hypersonic vehicle can become surrounded by a complex plasma which may then react with the vehicle surface in several ways. The plasma surrounding the Apollo re-entry vehicle is a classic example in which ionization of the surrounding air makes a radio communication "black out" inevitable.

Problems

Not all these difficulties occur simultaneously and many early design studies concentrated on hypersonic airliners with air breathing engines, capable of Mach numbers between 5 and 12, depending on the range required. The first practical example of a manned hypersonic vehicle will, however, be the re-usable space shuttle, although the North American X-15 research aircraft has flown at $M=6$ under rocket power. The chief aim of this article is to emphasize some of the problems common to all hypersonic vehicles, to describe some of the relevant research in the Aeronautics Department of Imperial College and to outline the solutions to these problems that are likely to be adopted in the case of the space shuttle.

The greatest single problem in hypersonic flight is the kinetic heating of the structure by the surrounding mass of hot air; the air is heated by the motion of the vehicle. In the case of Apollo a high drag shape is used to convert all the kinetic energy of the re-entry capsule into heat through a very strong bow shock wave. For a long range airliner the design aimed for would be a low drag shape generating much weaker shock waves, but very high temperatures would be generated by skin friction in the boundary layer. In both cases the problem is the same insofar as most of the heat generated in the air must be prevented from weakening the structure or harming the occupants. There are many ways of doing this. The most obvious is to clad the load bearing structure with a heat shield which can ablate during the flight. New alloys using exotic and expensive metals or carbon compounds are under

extensive development in the hope of making a structure which can retain its strength at elevated temperatures. Active cooling can be employed either internally or externally, using the fuel indirectly as a heat sink or directly as the coolant film. The last of these solutions is unlikely, except in the engine, for autoignition of the fuel can occur at high temperatures. Experience with the ill-fated North American Valkyrie Mach 3 bomber showed how difficult it is to build a leakproof, fuel-filled wing structure.

No matter which of the many thermal protection schemes is adopted there will be a substantial weight penalty and accurate knowledge of the surface heat transfer rate is required. This in turn requires extensive fundamental information concerning the behaviour of the boundary layer under many different operating conditions.

The second challenging problem is that of propulsion. Even Concorde, the fastest airliner yet built, can operate quite efficiently throughout its speed range, $0 < M < 2.2$, using just one type of air breathing engine. At higher Mach numbers all the compression needed can be obtained from the ram effect alone and the turbine driven compressor of the conventional gas turbine is unnecessary. A ram jet is far more

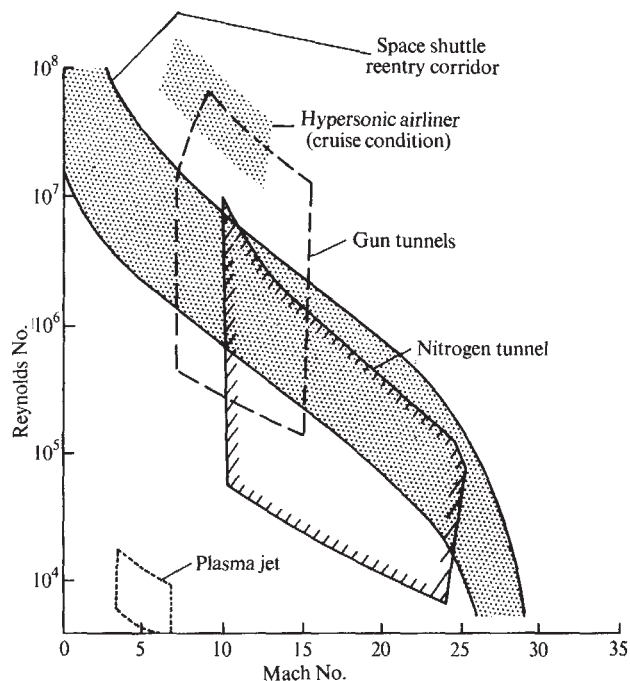


Fig. 1 Comparison of hypersonic facilities in the Aeronautics Department of Imperial College. The altitudes corresponding to the Reynolds numbers are, very approximately, 400,000 foot (10^4), 300,000 foot (10^5), 200,000 foot (10^6), 100,000 foot (10^7), 0 foot (10^8). The exact values of the conversion factors depend on the flight pattern chosen.

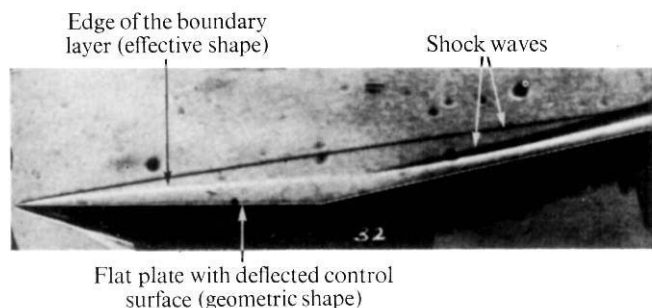


Fig. 2 Laminar boundary layer growth at $M=14.5$; flap deflexion $=13^\circ$

efficient. At extreme altitudes a rocket which carries its own fuel is the only possible propulsion unit. Thus the hypersonic vehicle which has to take off and land under its own power must either carry several engines, each very efficient in a limited part of the range of Mach number range, or use one engine which will be inefficient for some part of the mission. Again the consequence is a large weight penalty either in duplicated propulsion units or in the fuel required.

The drag of an aircraft rises at supersonic speeds because the pressure waves generated by the vehicle can no longer travel ahead. Instead they coalesce to form shock waves which change the pressure distribution around the aeroplane and cause wave drag, which is in some ways analogous to the surface wave drag of a ship. Although the increase in drag can be alleviated by sweeping the wings back inside the Mach cone at supersonic speeds, the cone becomes too narrow at $M > 5$ for such a highly swept wing to maintain adequate lateral control. Inevitably the ratio of lift to drag is reduced and a hypersonic vehicle will do well to reach a value of L/D of 5, which should be compared with the current value of 15 for modern subsonic airliners. The corresponding ratios of installed takeoff thrust to takeoff weight are approximately 1 and 0.25 respectively.

All these considerations entail large weight penalties and it requires considerable ingenuity to produce a design having a worthwhile payload. The trend is already discernible—the Boeing 747 “Jumbo” Jet has a payload of 32% whereas Concorde’s is 8%. One simple, effective but expensive way of solving this problem is by staging. The first stage lifts the payload carrying vehicle to a speed and altitude from which it can complete the mission and then detaches and returns to base. This is really just a more sophisticated version of the extra fuel, drop tank principle.

Research at Imperial College

Four hypersonic facilities are currently in use at Imperial College; their capabilities in terms of space shuttle and cruise vehicle flight patterns are shown in Fig. 1. The two gun tunnels are intermittent with a test time of a few ms; they are variations of the shock tunnel and operate rather as a one stroke bicycle pump. Compressed air, stored at up to 1,000 atm in the high pressure section of a long tube, is used to drive a free piston down the remainder of the tube by suddenly rupturing metal diaphragms separating the two sections. The acceleration of the piston generates a strong shock wave which reflects from the closed tube end, and reflects again from the moving piston; the process continues so that the gas ahead of the piston is compressed and heated by multishock reflexion. A second diaphragm in the end of the tube then opens to allow this hot reservoir of gas to expand through a convergent-divergent nozzle to hypersonic speeds, at which stage it flows over the model and into a dump tank. Fast response transducers, resistance thermometers and sensitive strain gauges enable measurements of pressure, heat transfer rate and overall forces to be made.

By contrast, the nitrogen tunnel and plasma jet are continuous facilities with extensive water cooling which allows them to run for hours if necessary. The nitrogen tunnel passes very pure high pressure N_2 through an electrically energized graphite heater capable of raising the temperature to 3,000 K; it then expands through a nozzle to very low pressures and a Mach number of 20. The tunnel operates in the transitional regime between free molecule and continuum flow. The mean free path of the molecules in the test section is typically 0.1 mm. Diagnostic techniques include an electron beam for measuring density and temperature. The plasma jet generates a similar mean free path length in argon at $M=6$ by heating the gas initially to 12,000 K in a settling chamber across which an intense arc is struck. The tunnel has most recently been used for studies of an ionized boundary layer.

The gun tunnels and the nitrogen tunnel are also being used to study hypersonic boundary layers so that pressure and heat transfer rates may be predicted more accurately¹⁻³. At hypersonic speeds the mean temperature in the laminar boundary layer is so high, and the density therefore so low, that the layer is thick enough to significantly distort the outer flow and greatly modify the pressure distribution. The modified pressure distribution in turn influences the growth of the boundary layer. A good example of such strong viscous interaction is shown in Fig. 2 where there is a very large difference between the effective and geometric shapes.

Another important example of interaction occurs when a control surface is deflected so far that the shock wave generated is strong enough to cause boundary layer separation. The flow then leaves the surface ahead of the corner, only to reattach somewhere on the deflected control. Flow separation can lead to extensive changes in the local forces and heat loads so the conditions for incipient separation are crucial to any design. Fortunately the boundary layer becomes more resistant to separation at high Mach numbers and very large control deflexions may be permissible particularly if the boundary layer is turbulent (Fig. 3). Many two dimensional shapes have been used to provide experimental data against which a number of theories capable of predicting viscous and shock-boundary layer interactions can be tested.

The research programmes of a more applied nature are concerned with filmcooling a flat plate and heat transfer to both the windward and leeward surfaces of a delta wing. One method of surface protection is to inject a coolant film along the surface from a tangential slot, thus insulating the hot boundary layer from the wall. If the layer remains laminar then this method works well, but in turbulent flow the violent mixing rapidly destroys the coolant film.

In supersonic and hypersonic flight a delta wing is usually preferred to a straight wing design, for the centre of pressure does not move so much with Mach number. Moreover a very stable vortex flow is generated at low speeds ensuring

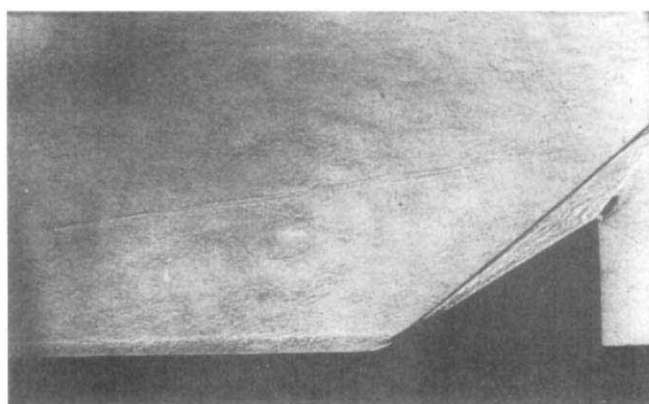


Fig. 3 Turbulent boundary layer growth at $M=9$; flap deflexion $=30^\circ$.

good handling at takeoff and landing. In hypersonic flow the flow is mostly three dimensional and quite complex. Force and pressure data^{4,5} are now to be followed by heat transfer measurements with particular emphasis on the high angles of incidence likely during the re-entry phase of a space shuttle.

Other research orientated towards the shuttle is a comparison between flat bottomed delta and caret delta wings (Fig. 4). Nonweiler⁶ showed how recessing the lower surface could under certain conditions lead to a purely two dimensional flow under the wing. This idea of using known flow fields and finding a shape to support them rather than drawing a shape and hoping to calculate the surrounding flow was extensively developed by the Royal Aircraft Establishment (RAE) in Britain. Recently Townend *et al.*⁷ have shown how recessing the lower surface of a space shuttle would increase the lift coefficient by reducing flow spillage around the leading edges. For the same lift either the flight altitude could be greater (lower density) or the flight speed could be reduced. Hence the heat transfer rate to the vehicle would be diminished.

The nitrogen tunnel is also being used to investigate the benefits of a caret wing at $M=20$ under conditions appropriate to the initial high altitude re-entry phase. Both the pressure distribution and overall forces are being measured. The United States is now showing signs of interest in these ideas which might then be incorporated in subsequent space shuttle designs.

In the structures laboratory, facilities for simulating the effects of kinetic heating include both radiant and induction heating plant. The power available is 360 kW from 120 quartz lamps and 25 kW at 1/3 MHz, respectively. Recent research has developed a technique for representing transient or cyclic thermal conditions in structural models by on-line computer control of the radiant heaters. Structural problems under investigation include the reduction in flexural and torsional stiffness which occurs in wedge shaped wings during the heating and cooling phases of flight.

There is of course a great deal of hypersonic research continuing elsewhere in Britain, in particular at RAE and the Universities of Oxford and Southampton.

Space Shuttle

Having outlined the difficulties of hypersonic flight and some of the current research it is interesting to look at the solutions adopted in one of the American space shuttle designs (Fig. 5). It must be emphasized that the design is still changing and that the comments here reflect progress to date.

In order to achieve the required payload of 65,000 pounds the vehicle is staged. The first stage is a pair of solid propellant rockets which lift the orbiter vertically and accelerate it to $M=7$ at 200,000 foot. The first stage is then detached and decelerated by parachute before landing in the sea. An alternative

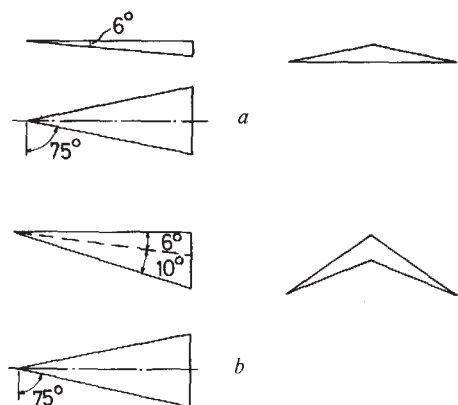


Fig. 4 a, Flat bottomed delta wing; b, caret delta wing.

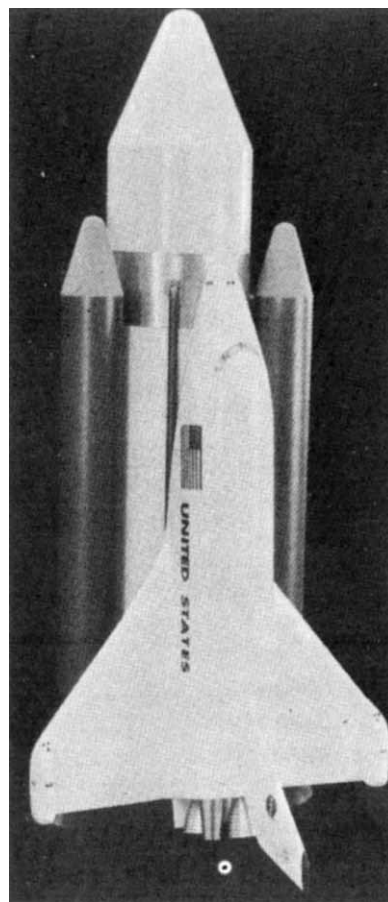


Fig. 5 A possible design for the space shuttle.

scheme uses hot air balloons inflated at very low altitude to bring the spent rockets to rest just above the sea. A sea anchor is deployed and the re-usable first stage later retrieved by boat. The orbiter comprises a manned, delta wing, rocket powered vehicle sitting on the back of a mammoth cylindrical fuel tank which is dumped in space when exhausted. To protect the structure⁸ during re-entry the orbiter uses a metallic heat shield over the entire lower surface, parts of the top surface and the whole fin. Shingles of columbium, nickel and titanium are used but for the extremely hot parts, the nose, the wing and fin leading edges, carbon may be employed. The ratio of lift to drag is about 2; enough to meet the requirement of 1,400 mile cross range which makes most of the United States a possible landing area. A retractable air breathing engine is incorporated for low altitude manoeuvre and landing.

The design then is a sensible, conservative but relatively expensive compromise. The heavy weight penalties of heat shielding and propulsion enforce a staged vehicle not all of which is re-usable. The aerodynamic performance is modest because of the specification which includes a lifetime of at least 100 missions with perhaps a total of 60 h of flight under hypersonic continuum conditions. It is certain that a more complex and sophisticated solution will be needed for the economic operation of a hypersonic airliner with the need for much more research not least into the problems of hypersonic boom.

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Periodicities in Seismic Response caused by Pulsar CP1133

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A seismometer/computer combination has detected seismic vibrations corresponding to the half-period of pulsar CP1133. A hitherto unknown pulsar may have been detected by the same technique.

A SEARCH for periodicities in seismic output which correspond to pulsars' frequencies was first made by Wiggins and Press¹. They analysed only 20.5 h of seismic data to see if a line split predicted by Dyson² was present, and give an upper limit to the amplitude of the ground motion of 10^{-2} pm or 10^{-9} cm.

We repeated their experiment with a much larger integration time, using a vertical seismometer (Rocard, Ecole Normal Superior, Paris) placed in a seismic station 15 km north of Eilat, Israel ($29^{\circ} 40' N$ latitude, $35^{\circ} E$ longitude). The seismometer is sensitive between 0.1 Hz to 10 Hz, and is connected through an amplifier which gives 0.5 V per 1 mm of vertical movement at 1 Hz to a correlator which digitizes the analogue

signal and performs an on-line autocorrelation. This technique suppresses the non-periodic noise and enhances any periodic signal.

The time range of the correlator, 0.1 s/channel, was chosen to detect the periods of known pulsars, 0.2 s–10 s. After 13,107 s of correlation, the 100 channels are printed, the memory erased and the analysis starts again. To obtain the power spectrum, a separate Fourier analysis is performed for each 13,107 s of data. The first ten channels of autocorrelation were dropped because they contain most of the noise. This does not change the period, but gives a better signal to noise ratio.

Periodicity of Data

After the first few days of data reduction, it became apparent that the power spectra showed a persistent peak which corresponds to a period of 0.53–0.60 s. (The uncertainty in the period results from the time-uncertainty for each channel.) Fig. 1 shows an example of an autocorrelation and its power spectrum where this peak shows best. After several weeks, we noted changes in the height of this power spectrum peak during the day, and to see the exact periodicity of these changes a Fourier analysis on the amplitude of the power spectrum which corresponds to the 0.53–0.60 s period was performed. This analysis shows an approximate 24 h period (Fig. 2). To distinguish between the sidereal and solar period, the times and dates

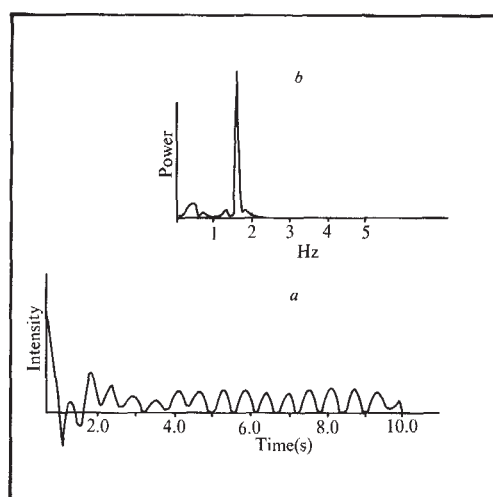


Fig. 1 Autocorrelation (a) and the power spectrum (b) obtained on December 19, 1971, between 2347 (local time) and 0325 on the 20th. (Local time=GMT+2 h.) The peak corresponds to a period of 0.53–0.60 s.

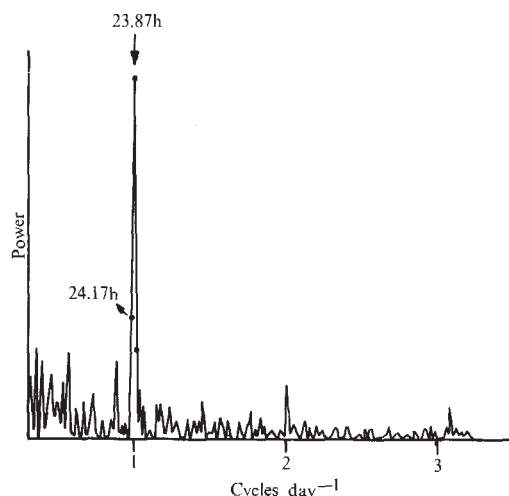
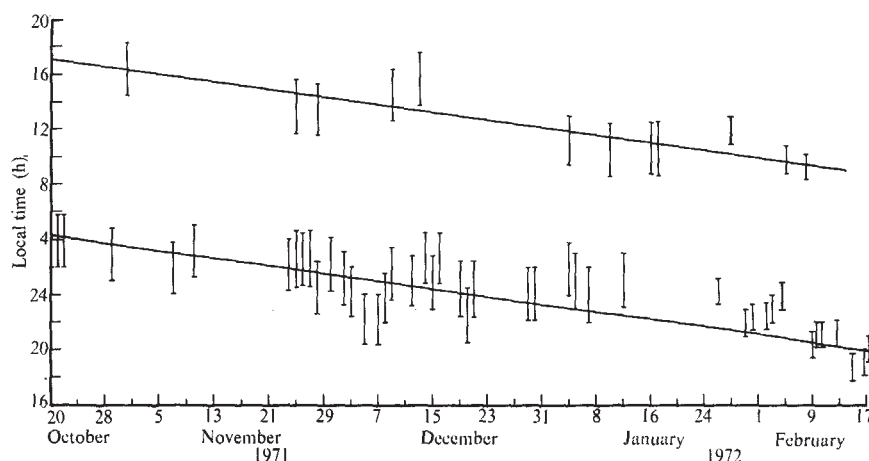


Fig. 2 Fourier components of the amplitudes of the power spectra which correspond to the 0.53–0.60 s period. 2387 h variations are apparent.

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Fig. 3 The time of the day when the maxima in the power spectra occurred is plotted versus the date. The line corresponds to the times when these maxima should occur if CP1133 emits gravitational waves.



when these amplitudes showed a maximum were determined. Two criteria were employed in determining these times. First, the amplitude had to be at least twice as high as the total sum of the rest of the channels, which corresponds to all the other periods between 0.1 s and 10 s. This criterion prevents us from considering times when noise was present, and thus subjective assessment of noise is eliminated. The second criterion is that at times before and after the maximum occurs, the amplitudes are at least half the amplitude of the maximum, ensuring that there is a gradual increase in the amplitudes and not just a one-time event. The difference between Fig. 2 and Fig. 3 is that in Fig. 2 all the data were used to perform the Fourier analysis and in Fig. 3 a selection, based upon the two criteria, was made. The error bars in Fig. 3 correspond to the integration time, initially 3 h 38 min, then later 1 h 49 min.

Fig. 2 shows that the precise periodicity is slightly less than 24 h. This is shown in a different fashion in Fig. 3 where the slope of the lines corresponds to a sidereal period; the points are consistent with these lines. It is evident from Fig. 3 that the maxima fall on two lines which are separated from each other by approximately 13 h. Fig. 2 does not show an 11 or 13 h period because there are seldom two consecutive maxima.

Determination of Exact Period

To find the exact period of the seismometer output, the correlator was used in the signal recovery mode. In this mode one chooses a precise period (by means of an external frequency synthesizer) and the seismic output is superimposed on the 100 channels with this period. We switched to this mode on March 6, 1972, using the exact period of CP1133, 1.18791 s, to trigger the correlator. The instrument was set up to record $2,048 \times 1.18791$ s of data, print the results and restart without losing phase. If the seismometer output repeats itself with

half the period of the radio pulsar, two peaks should show up separated by 0.59 s (Fig. 6). (If the period dialled into the trigger differs by 0.1 ms from the pulsar's period, the two peaks would have been smeared by 240 ms during the 2,400 s of integration.) The two peaks do not show up when the pulsar is overhead and when a totally different period is dialled into the trigger. The same two peaks were found on three different days, but they will show up only when the seismic noise is very low.

A brief statistical analysis is necessary in order to evaluate these results. The probability that random seismic output will show a peak in the power spectra as large as that seen in Fig. 1 is smaller than one part in 10^8 (number of channels times $e^{-S/N}$ where S is the height of the signal and N the average noise). The same calculation shows that the peak in Fig. 2 has a random probability of 10^{-7} . There is a probability of less than 1% that the maxima fall on a solar day line and not on the sidereal day line. The fact that the two peaks in Fig. 6 showed up at the same place for two consecutive times leads us to calculate that the random probability for this to occur is one part in 2,000.

To exclude the possibility that the seismometer could act as an antenna and detect the radio waves from the pulsars, it was clamped, but the amplifier and power supply to the seismometer remained on. Small pulses were detected, but the autocorrelation during those days yielded no periodicity. The second check was to turn off all the small motors in the control room (150 m away and separated by three air-tight doors from the seismometer room). No change in peaks was observed. External factors such as power stations or pipeline vibrations were also eliminated as causes of the peaks.

Gravitational or Electromagnetic Waves?

Can the effects described above be due to gravitational waves from the pulsar CP1133? Weber, who pioneered a search for gravitational waves³, calculated the response of the Earth to gravitational radiation from pulsars⁴. He uses an example⁵ of the interaction of a gravitational wave with four point masses. The gravitational wave causes the masses, if they are aligned perpendicular to the direction of the wave, to vibrate at the frequency of the wave. If the masses are aligned in the direction of the wave, they do not move with respect to each other. This implies that if gravitational waves are emitted from a specific direction in the sky, all points on Earth which lie on a plane perpendicular to this direction will be excited, or a particular point on Earth will feel maximum vibrations twice a day as it crosses this plane. This will happen twice in a sidereal day or twice in 23 h 56 min.

The results shown in Fig. 3 are consistent with these predictions; if there was a source of gravitational waves at the position of CP1133 their effect on a seismometer in Eilat will be such as to give the maxima on the two lines plotted in Fig. 3.

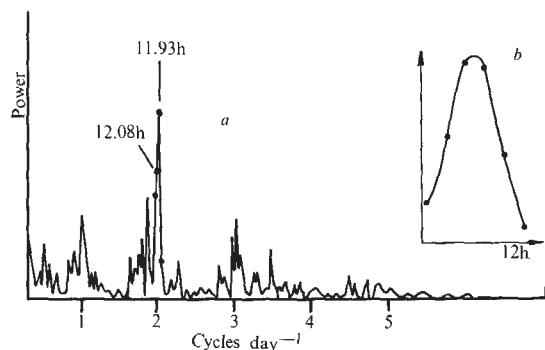
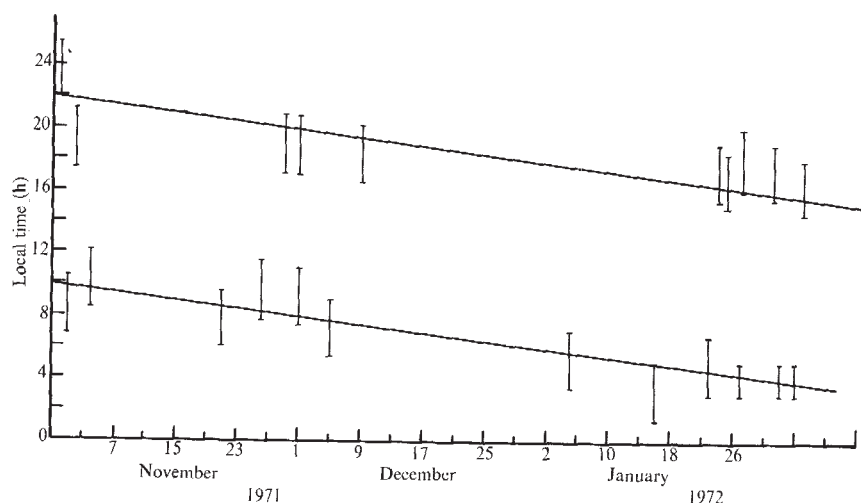


Fig. 4 *a*, As Fig. 2, but for the period of 0.33–0.34 s. *b*, Typical change, during 12 h, of the amplitudes of the power spectra for the period of 0.33–0.34 s.

Fig. 5 As Fig. 3 for the period 0.33–0.34 s.



Two more pieces of evidence support the suggestion that we are detecting this pulsar. Its period, as measured in the radio-frequency region, is 1.1879 s. If the radio waves are emitted once for each rotation of a rod-type mass, the period of the gravitational wave will be half of the radio period⁵, 0.594 s. The period observed, 0.53–0.60 s, is consistent with this period. Secondly, CP1133 is the second nearest pulsar to Earth (80 pc) and thus would have the greatest effects. The nearest pulsar, CP0950, which has a 0.253 s period in the radio frequency or 0.126 in gravitational waves, could not be detected by our equipment because of the 0.1 s channel width. In order to detect CP0950, a narrower channel width is required.

On the other hand, the amount of Earth's displacement due to gravitational waves from pulsars as calculated by Weber⁴ and Dyson² is of the order of 10^{-17} cm as compared with 2×10^{-9} cm found in this experiment. Thus, without an amplification mechanism in the Earth's crust and if pulsars have the properties used in the calculation, the effect found here is not due to gravitational waves. Several arguments can be raised as to why the effect cannot be due to the electromagnetic

radiation from pulsars. We do not know of any other mechanism that can cause the effect described here.

A New Pulsar?

When analysing other periods for daily variations, the period 0.33–0.34 s showed a clear 12 h variation as seen in Fig. 4. The times of its maxima are plotted in Fig. 5. The two lines drawn are the best fits to the data and they do not correspond to any known pulsar. However, in principle, a pulsar with a radio period of 0.67 s could be responsible because radio emission from pulsars is highly directional and gravitational emission is not. Therefore, one should expect to detect more gravitational pulsars than radio pulsars. The right ascension of this presumed pulsar is either 06 h 50 min or 18 h 50 min as we cannot distinguish between those two right ascensions.

It is difficult to estimate the amount of the Earth's vertical displacement which occurred in each case. As the original pulse is not retrievable in our technique and we have only its autocorrelation, we cannot know if the vibration was present for 3 h 38 min or only part of this time. If we assume a noise level of 8×10^{-8} cm, our estimate of the instantaneous vertical displacement which corresponds to the peak in Fig. 1 is 2×10^{-9} cm.

It must be remembered that the ability of the system to detect a non-terrestrial periodic event depends on the Earth's own noise. For times when the seismic noise (caused by the Earth or human disturbances) is high, the sensitivity decreases. This could be the reason why there are days when no signal is detected and why there are more points on the midnight line (lower line in Fig. 3) than on the midday line. It could also explain why the effect was not detected by Wiggins and Press¹ during the 20.5 h of their experiment. On the other hand, there is a possibility that the station in Eilat is better as it is "seismically isolated by faults from its surroundings, and in which a gravitational wave may excite resonant standing vibrations"², whereas the LASA¹ station is not.

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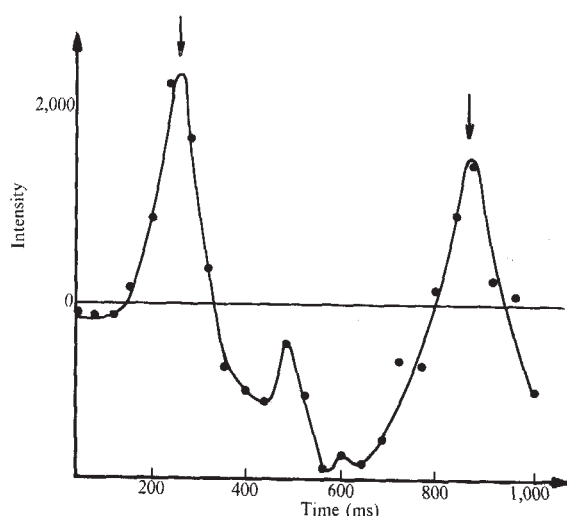


Fig. 6 The "light curve" for CP1133 (taken on March 7, 1972, 1804 LT). It represents the superposition of 2,048 consecutive repetitions of the seismic data with the precise period of 1.1879 ± 0.0001 s. The time between the arrows is 0.59 s. The seismic output has precisely half the period of the radio pulsar. (Because the repetition rate is 1.1879 s and the channel width is 0.01 s, the last 0.18 s are lost and, therefore, not shown.) Intensity in arbitrary units; the maximum ground motion is estimated to be 2×10^{-9} cm.

Possible Sidereal Period for the Seismic Lunar Activity

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Maximum lunar seismic activity corresponds to the rise of the pulsar CP1133 at the site. Other agreement with Earth based experiments suggests that they have a common origin.

STRIKING similarities exist between the lunar seismic response of the Apollo 12 vertical seismometer as reported by Latham *et al.*¹ and the response reported by Sadeh *et al.*² in the preceding communication. The Apollo 12 station has been operating since November 1969, and moonquakes have been recorded for more than two years. The interesting feature of this seismic activity is its periodicity, of approximately 27 days. This is seen in the upper part of Fig. 1 (taken from

perigees is 27.554 days. The nodical month or the time between two nodes is 27.212 days. The sidereal period or the rotation of the Moon as seen by a fixed star is 27.321 days.

Effect of Pulsar CP1133

In Fig. 1b the dates of occurrence of the maximum activity are plotted with respect to the time of perigee. If the effect is correlated to perigee, the points should have been on a horizontal line. If the effect is due to an object outside the solar system, it should follow a sidereal lunar period. The line drawn corresponds to the lunar sidereal period and corresponds to the position in the sky of the pulsar CP1133; this pulsar is in the horizon for the location of Apollo 12, at the time of maximum activity.

The published data for 1970, as presented in Fig. 1, are not conclusive enough to distinguish between the sidereal period

Fig. 1 *a*, Total lunar seismic energy as a function of time for the year 1970 where a 27 day period is clearly seen. *b*, Interval between perigee and the time of occurrence of the maximum seismic activity. Ordinate is days before perigee. The line is the sidereal lunar period and it corresponds to the rise of the pulsar CP1133 in the Apollo 12 site.

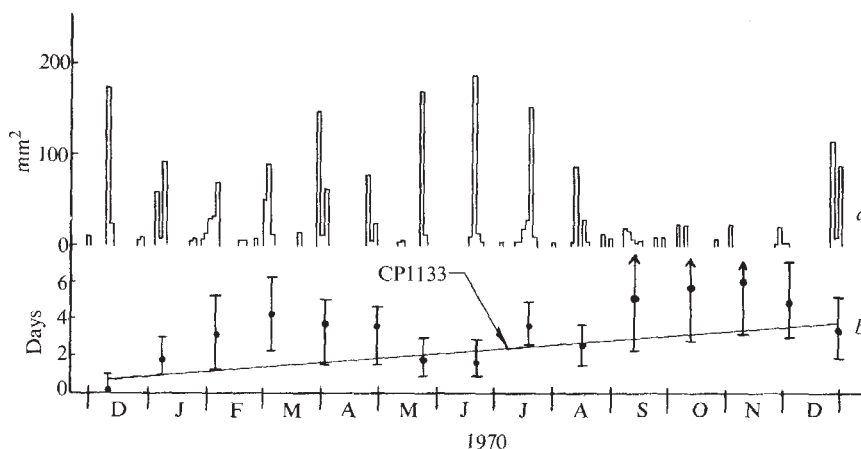


Fig. 4, ref. 1) where seismic activity is plotted as a function of time. As the exact days of maximum activity are known, it can be correlated with known characteristic periods of the Moon. The anomalistic month or the time between two

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and the anomalous month. Unpublished data, supplied by the Lamont-Doherty group, for the 1971 events agree well with the sidereal period and rule out the anomalous month period. It can still be a nodical month period, but this period has only a geometrical and no physical meaning.

One other similarity between the lunar¹ and Earth based

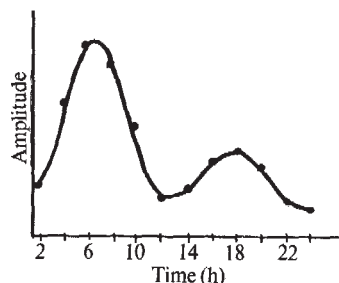


Fig. 2 Amplitude of the Fourier components which were found for the Earth based experiment in Eilat for the 0.33 s pulsar as a function of the time of the day. It represents a superposition of 10 days in order to achieve high significance.

experiment² is the fact that when a star rises at the seismometer location, the seismic response is higher than when the star sets. This is seen in the upper part of Fig. 1 where between almost every 27 day peak there is a smaller peak and in Fig. 2 where the data obtained in Eilat² are plotted. To obtain this plot, 10 days were superimposed to give a more significant analysis. It is not hard to explain this fact if the gravitational wave is polarized.

In conclusion, three of the predicted effects due to gravitational waves are present in the lunar seismic data. (1) A sidereal period (which even without reference to gravitational

waves is an interesting observation). (2) It appears twice in a lunar day. (3) It corresponds to the position in the sky of a nearby pulsar. It has still to be proven that the period is the same as the pulsar's.

Further Proof

One other proof will be if the seismic activity for the Apollo 15 station peaks two days later than the Apollo 12 station. The individual events could be confusing because they can be genuine moonquakes. Gravitational waves should arrive at all the stations at the same time, but at a different intensity depending on the position of the star with respect to the station. One mechanism to explain why individual events are recorded can be that the gravitational waves trigger a genuine moonquake and, therefore, the integrated activity has a maximum at the right time while the individual quakes are random.

The gravitational wave interpretation of the lunar seismic response has the same drawback as the Earth based experiment; namely, the effect is orders of magnitude larger than the theory predicts.

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Search for Seismic Signals from Gravitational Radiation of Pulsar CP1133

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Attempts to derive seismic signals from CP1133 were unsuccessful. Possible experimental errors in previous work are discussed.

THEORETICAL estimates^{1,2} of the seismic response of the Earth to gravitational radiation near 1 Hz indicate that the surface displacement of the Earth should be about 10^{-17} cm in response to a source of gravitational waves with energy flux equal to that of a star of bolometric magnitude zero. Since microseisms at an optimally quiet seismic station will produce ground motions of 10^{-8} cm or more (for a 10 Hz bandwidth)

the noise is nine orders of magnitude greater than the expected signal. Nonetheless Dyson suggested that a search for such signals would be worthwhile since the estimates involved possible uncertainties of several orders of magnitude. Following this suggestion, Wiggins and Press³ analysed 20.5 h of data from a large seismic array in Montana, USA. They searched for signals from four nearby pulsars and concluded that if such signals exist the Earth's response must be less than 10^{-9} cm in amplitude.

A great deal of excitement has been generated recently by the announcement by Sadeh and Meidav⁴ regarding the possible detection of a seismic response of the Earth to gravitational waves from the pulsar CP1133. Using an autocorrelation analysis of about five months of seismic data, they conclude that they have observed signals emanating from a position in the sky that agrees with the known position of CP1133. They estimate the signal to correspond to a ground displacement of 10^{-10} cm. They also performed a signal-average at the known pulsar period of 1.18791 s; they believe that the appearance in a 2,048 period signal-average curve of peaks at half the pulsar period proves the signal they observe is synchronous with the pulsar to four decimal places.

Experimental Set-up

We report here an analysis of signals from a seismometer located near Jamestown, California. Following Sadeh *et al.*, we have limited our initial effort to a search for CP1133. We used a 14 kg Benioff vertical seismometer ('Geotech model 4681') located in a tunnel in the foothills of the Sierra Nevada mountains. The signal was amplified at the site with a phototube amplifier (10 Hz bandpass), frequency modulated, and sent over telephone lines to our analysis station in Berkeley, California, where the signal was de-modulated, amplified, and filtered, reducing the bandwidth to approximately 5 Hz. Fig. 1 shows the relative gain of the entire system as a function of frequency. The seismometer calibration was checked several times each day with a magnetically induced impulse to the inertial section; no change in calibration was observed during the running period.

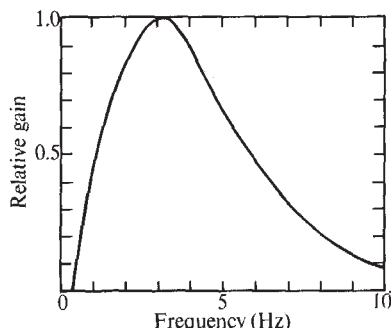


Fig. 1 The relative gain of the seismographic, amplification, and filter system as a function of frequency.

Throughout our analysis we have used signal-averaging to search for signals at the apparent frequency of the pulsar. Signal-averaging is a sensitive technique for extracting from noise a signal of arbitrary shape but known period. The

averaging was done with a 1,024 channel multiscaler triggered by a frequency synthesizer set at half the pulsar frequency. The multiscaler adds the records of consecutive sweeps; signals at the pulsar frequency and its harmonics add coherently while signals at other frequencies add incoherently. Thus the signal-to-noise ratio increases in proportion to the square root

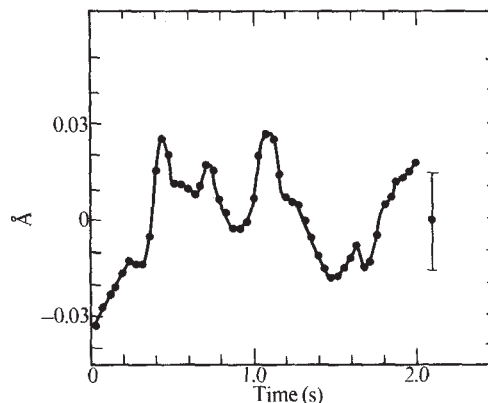


Fig. 2 Ground displacement averaged for 30,333 two-second periods, synchronized at half the frequency of pulsar CP1133. The apparent pulsar period, corrected for the motion of the Earth, is 1.187983 s. The vertical bar indicates the expected r.m.s. of the entire curve, calculated by dividing the average noise by the square root of the number of sweeps. The vertical scale is calculated from the known gain of the system at 2 Hz.

of the number of sweeps. Because of the quadrupole nature of gravitational radiation, the period observed should be half that seen in the electromagnetic spectrum, about 0.59 s. Each sweep of the multiscaler was 2 s in duration. (At the end of a sweep there was a dead-time of approximately 0.38 s before the next trigger pulse arrived.) One would expect the pulsar signal to repeat itself about 3.4 times within one sweep. The pulsar frequency used was calculated from the intrinsic pulsar frequency⁵ by correcting for the Doppler shift⁶ due to the motion of the seismic station relative to the centre of mass of the solar system. The average Earth noise was measured before, during, and after signal-averaging runs, using a pulse height analyser. The Earth noise was approximately Gaussian with a half-width at half-maximum that varied from 3×10^{-8} cm $\text{Hz}^{-1/2}$ during the day to about 1×10^{-8} cm $\text{Hz}^{-1/2}$ at night and at weekends. To reduce fluctuations due to earthquakes, the signal into the multiscaler was limited at about three times the average noise level. (Although ground motion in excess of this limit occurs less than 1% of the time, such motion, if not limited, can greatly increase the average noise.)

No Signals from CP1133

Fig. 2 shows the average ground motion for 30,333 sweeps synchronized to half the pulsar frequency. This represents our quietest and longest running period of approximately 16 h (April 15–16) when the Earth noise was approximately 1×10^{-8} cm $\text{Hz}^{-1/2}$. A true signal from CP1133 would appear in this signal average as three peaks about 0.59 s apart. No such set of three peaks is observed. The vertical bar indicates the expected r.m.s. deviation for the entire curve based on the measured noise. The deviations observed are con-

sistent with those expected from noise; no pulsar signal is detected.

Fig. 3 shows an average signal from 31,850 sweeps taken during a noisier period. Once again the observed fluctuations are no greater than expected from Earth noise. It is interesting to note that if a signal were present, it should appear with the same shape in both Figs. 2 and 3. No such similarity is seen. Fig. 4 shows the average signal for 23,050 sweeps when the frequency synthesizer was set approximately 1% different from the known pulsar frequency in order to check our understanding of the Earth noise. Again the r.m.s. deviation is consistent with that expected.

More than 35 signal-averaging runs have been made (most of them for fewer sweeps than the data in Figs. 2-4). For these runs, precedence was given to those times of day when the signal from the pulsar was expected to be at maximum, that is when the pulsar was on the horizon as seen from Jamestown. In all our runs the observed fluctuations are attributable to noise. If there is a seismic signal due to pulsar CP1133 its r.m.s. amplitude at our seismometer must be less than 10^{-10} cm.

Possible Errors in Sadeh *et al.*

The results of our experiment conflict with those of Sadeh *et al.* We think that their signal estimate of 10^{-10} cm is too small to be consistent with their reported noise level, their technique of analysis, and the data shown in their figures. During a quiet period their ground noise was as low as 10^{-8} cm (3×10^{-9} cm Hz $^{-1/2}$) (ref. 4 and private communication). From this value we can calculate the sensitivity of their experiment.

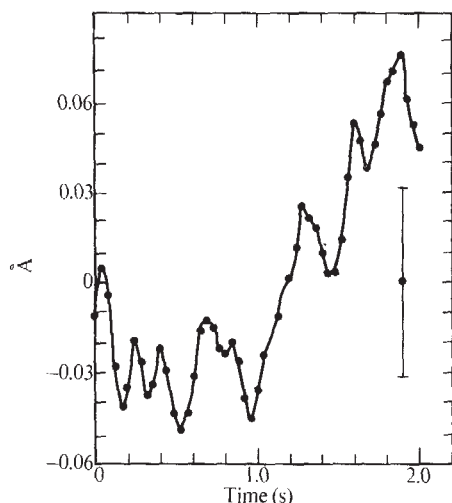


Fig. 3 Ground displacement average, similar to that in Fig. 2, but during a noisier period.

In the Fourier analysis of their autocorrelation data Sadeh *et al.* have a bin width of 0.53-0.60 s. Thus they cannot distinguish frequencies within a bandwidth of $1/0.53-1/0.60=0.2$ Hz which is their operating bandwidth. Because the autocorrelation technique improves the signal power/Earth noise fluctuation ratio by a factor of $\sqrt{1,310}=36$ and the ratio of signal amplitude to random Earth noise fluctuation to $\sqrt{36}=6$ they should be able to see in their studies signal six times weaker than their Earth noise (3×10^{-9} cm/Hz) $\times (0.2 \text{ Hz})^{1/2} =$

1.3×10^{-9} cm; thus the minimum detectable signal (signal-to-noise=1:1) would be 2.2×10^{-10} cm. The criterion for accepting a signal as significant was that the amplitude in the pulsar channel in the Fourier spectrum "had to be at least twice as high as the total sum of the rest of the channels (which corresponds to all the other periods between 0.1 s and 10 s)" (ref. 4 and private communication). In the autocorrelation plot the signal stands out strongly. Thus it must be far above their minimum detectable signal of 2×10^{-10} cm, and therefore much greater than our limit of 10^{-10} cm.

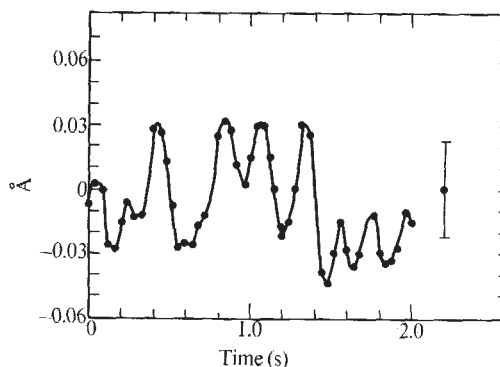


Fig. 4 Ground displacement average, similar to that in Figs. 2 and 3, but synchronized at a frequency approximately 1% different from the half-frequency of pulsar CP1133. Any true pulsar signal would therefore be washed out. Period = 1.202261 s.

From signal-averaging runs Sadeh *et al.* report a strong signal after 2,048 sweeps (2,048 pulsar periods, since their sweep time was 1 s, followed by 0.19 s dead time). Their noise per $\sqrt{\text{Hz}}$ was a factor of 3 lower, but we operated with a narrower bandwidth (5 Hz vs. 10 Hz); thus their Earth noise may have been as low as half our Earth noise and we need approximately four times as many sweeps for equal sensitivity. In the present experiment runs with more than 30,000 sweeps (60,000 pulsar periods) show no signal above noise. It is incorrect to conclude, as was done by Sadeh *et al.*, that the appearance of peaks in a signal-average plot, separated by half a pulsar period, is either a verification of the detection of a pulsar signal or an accurate measurement of the pulsar frequency. Both Figs. 2 and 4 in this paper have peaks separated by approximately half the pulsar period, but in neither case may we accept these peaks as evidence of pulsar signal. In Fig. 2 the expected third peak does not appear, and all fluctuations are consistent with noise. Fig. 4 was taken from a run whose synchronization was not at the pulsar frequency.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Visual Observation of Electric Sparks on Gypsum Dunes

ELECTRIFICATION in dust storms has been studied at White Sands National Monument in southeastern New Mexico. In this region of New Mexico gypsum dunes, some of which are up to 10 m high, cover an area of about 690 km² and constantly change shape with the prevailing southwest winds.

The observations reported here consisted of measurements of atmospheric electric potential gradient with a radioactive probe at ground level, space charge by the filtration technique suggested by Obolensky¹ and Moore *et al.*², and wind speed with a three-cup anemometer, at 1.25 m above the ground. Atmospheric temperature and relative humidity were measured with a psychrometer at ground level. The apparatus was installed on top of the dunes or on the plane rugged areas between the dunes³.

I made a fascinating observation of electrical activity on May 11, 1971, when a thunderstorm passed over the site. Strong winds were blowing large quantities of sand into the air, and atmospheric temperatures were lower and relative humidities were higher than usual for the month of May in that region.

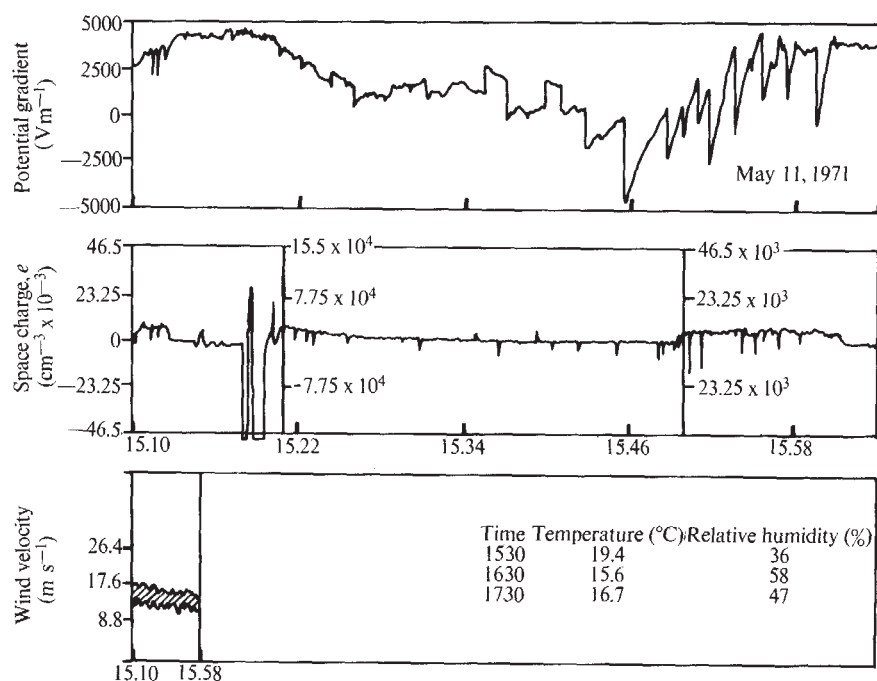
The apparatus was set up on a rugged surface about 10 m downwind of an 8 to 10 m high dune. The recording started at 1510 MDT (Mountain Daylight Time) when the strong winds were already blowing sand into the air. Electric sparks were observed extending from the top of the sand dunes up into the air terminating at a height of a few metres. At least five sparks, all on different dune tops, were observed within the period

1510 to 1600 MDT. These sparks extended straight up, and no branches were observed. The atmospheric potential gradient record made during this period shows some very rapid field changes (Fig. 1), which are both positive and negative. One of the sparks that occurred at 1535 MDT corresponded to a positive potential gradient increase of 1,500 V m⁻¹. Corresponding rapid changes in space charge density observed during this period are presumably due to some displacement current through the space charge tube.

In one type of field change (Fig. 1), occurring after 1545 MDT, the electric field changes and then exponentially recovers to its original value, which is typical of a field change caused by a lightning discharge. In the second type, occurring before 1545 MDT, the electric field changes and does not necessarily recover its original value. This second type of field change is presumably caused by the electric sparks on the tops of the sand dunes, and the first type is the result of lightning discharges in the thunderstorm. The fact that the darkest region of the thunderstorm was over the site of measurement between 1545 and 1625 MDT tends to confirm this idea. From 1630 to 1705 MDT precipitation was observed in the form of occasional light showers.

In interpreting the observed phenomenon, it is important to consider that, first, no such sparks were observed on two other days when strong winds were blowing considerable quantities of gypsum into the air but when no thunderstorm was nearby; second, in a series of laboratory experiments⁴, when gypsum powder collected from the same site was blown into a Faraday cage, very little space charge was produced, and it lasted for much shorter durations than those of sand or dust powders containing quartz and clay minerals. Further investigations,

Fig. 1 Recordings of atmospheric potential gradient, space charge and wind velocity on May 11, 1971, on a plane surface between the gypsum dunes at White Sands National Monument in New Mexico.



however, are required to understand fully the cause and characteristics of the sparks.

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Ball Lightning

A PHOTOGRAPH purportedly of ball lightning was taken by Mr R. C. Jennings and has been published several times¹⁻⁴ (Fig. 1). The path of the "ball" shows a pulsation that aroused our curiosity, and because a verified photograph of ball lightning would be of great value in understanding this phenomenon, we have investigated Mr Jennings's photograph and the circumstances under which it was taken.

In taking his lightning photographs Mr Jennings lay face down on a bed and held the camera against a window frame with the shutter open. After a lightning flash occurred, he closed the shutter, advanced the film, and made another exposure. Because of his position he could not see the scenes he photographed.

By examining photographs of the location, using a large scale map, and consulting the local electricity board, we were able to identify the bright flare at the left side of the print with the position of a 140 W sodium vapour lamp to an accuracy of about one foot. Mr Jennings states that the street lamp was off when the photograph was taken, between 0100 and 0200 h GMT in August or September 1961, but the Yorkshire Electricity Board stated that at this time of year the street lamps went on at about 2100 h and off at 0500 h; so the lamp should have been on when the photograph was made.

The image of the illuminated telephone kiosk appears "smeared" in the same direction as the apparent motion of the "ball" in the region of the bright flare. A small, bright spot of reflexion on the wet top of the kiosk formed a short trace showing the same modulation as the main trace. Its direction is consistent with both traces having been produced by camera movement, and is not consistent with a reflected image of the track of a pulsating and moving source. The colour of the "ball" and type of pulsation appear to be the same as those obtained by photographing a sodium vapour lamp at night with an open shutter and moving camera.

In the photograph there is a black shadow with a diffuse vertical edge covering part of the sky on the right-hand side. The trace of the "ball" passes across the shadow. In the original photograph 5 pulses of the trace are in the shadow but some reproductions have cut off the extreme edge. It is probable that the shadow was caused by a window edge or similar obstruction near the camera. The presence of pulses in the shadow area is a very good indication that the trace of the "ball" was inadvertently recorded by camera movement with an open shutter and not by something in the main scene. We suggest that Mr Jennings accidentally held his finger still on the button when he moved the camera to wind on the film—or a mechanical fault held the shutter open for a short while during the camera movement.

There is one point that is not explained by the street lamp hypothesis. Ball lightning often disappears with a loud report, and damage due to a lightning ball has been recorded⁵⁻⁷.

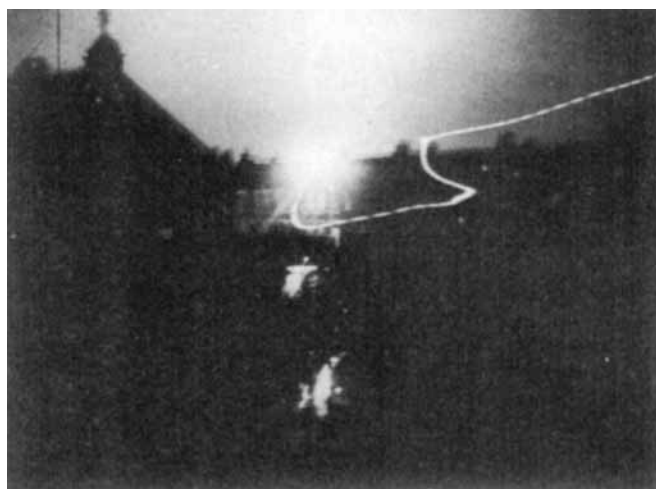


Fig. 1 Purported ball lightning photographed by R. C. Jennings. (Courtesy F. W. Lane.)

In this case Mr Jennings states¹ there was a "tremendous explosion" that caused him to move the camera. But he did not have any idea what he had photographed, and was surprised to see the picture, so the bang cannot be identified with certainty with this particular picture.

We conclude that the evidence is stronger for interpreting Mr Jennings's photograph as that of a street lamp than as that of a lightning ball. If this photograph does not add to the evidence for ball lightning, nor does it subtract from it. We suggest any future photographic evidence of ball lightning be examined soon after the event and as thoroughly as possible.

We thank Mr R. C. Jennings and Mr F. W. Lane for their assistance in this investigation and Professor Bernard Vonnegut for his support. The work of one of us (R. B. S.) was supported by the Office of Naval Research.

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Disclinations in Folded Structures and Geological Strata

DEFORMATION of rocks on a large scale¹ and laboratory scale² produces a variety of flow patterns which have been extensively discussed. These observations show that the wide variety of macroscopic patterns introduced by plastic deformation are very similar to those introduced in more nearly homogeneous materials such as single crystals. These configurations, especially those in single crystals, have been extensively explained in

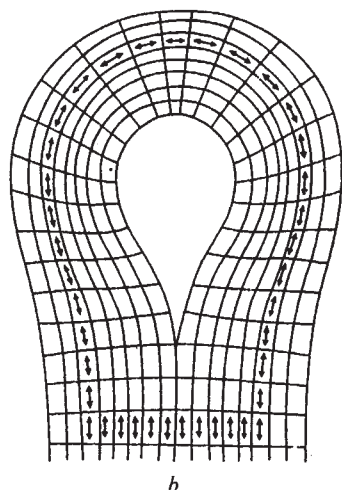


Fig. 1 *a*, Anticline which has been formed through a folding operation. *b*, A positive screw disclination (after Nabarro)⁴.

terms of dislocation theory^{3,4}, with a great deal of success. Some recent experiments on silver crystals have shown that disclinations can exist in special metal structures⁵. This has led me to consider if any of the folded structures in rock structures can be associated with typical patterns of disclinations. Here, I present a striking example of a structure which is consistent with a disclination and point out that the introduction of such figures might play a role in subsequent deformation patterns.

The pattern which I use to illustrate the point (Fig. 1*a*) can be compared to a positive screw disclination⁴ (Fig. 1*b*). The strata have folded and some of the folding operations have apparently led to a pinch off of some of the layers. Additional examples can be seen in the flow patterns of Paterson and Weiss².

The characteristics of a disclination, shown in Fig. 1*b*, are that it involves a rotation of the material in which it is embedded. The more familiar dislocation, on the other hand, involves a translation of the body. Thus, in Fig. 1*a*, one can distinctly observe flow patterns which have been rotated when flow occurs in the immediate vicinity of the anticline.

If these structures are the result of deformation by folding, can they influence the subsequent deformation process? Because a disclination involves a rotation of material relative to the surrounding material, especially in the case of a disclination loop, its expansion increases the extent of rotated

material. This suggests that the direction of the flow patterns in a medium will be shifted by the motion of disclination loops. Some aspects of the flow pattern in Fig. 1*a* are consistent with such an explanation. In order to accommodate this increase in material which is rotated during plastic flow, the flow might be turbulent in effect (as opposed to laminar flow in Cottrell's⁶ notation) and this turbulent flow might have as its source the rotation associated with disclinations. Another way of considering the disclination and its effect on the flow problem is to look upon the disclination as a gear which rotates the flow lines as they pass through it. Quite simply, if a loop, of radius r , rotates a flow line through an angle θ , when a layer is within a distance r of loop, this can then lead to crossing of flow layers. Such crossing of flow layers might introduce plastic buckling and cracking, which are important processes in geologic structures.

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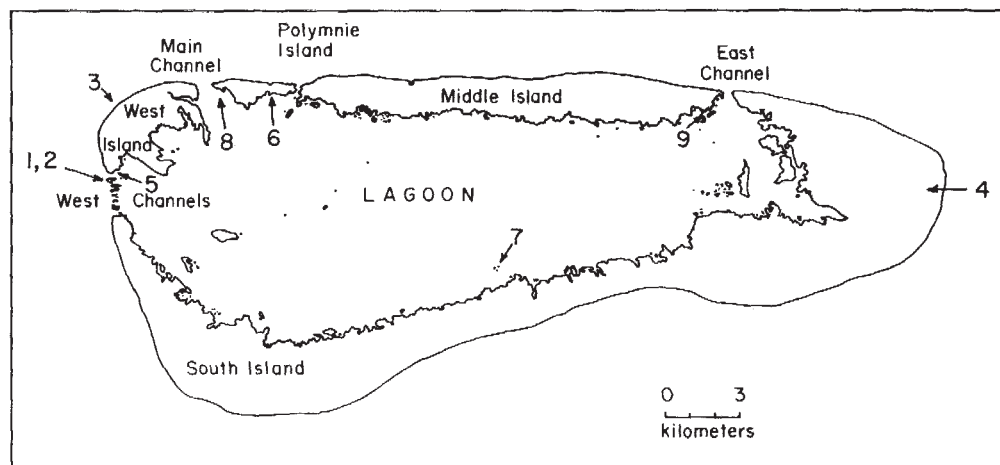
Redetermination of Chronology of Aldabra Atoll by ²³⁰Th/²³⁴U Dating

THE elevated coral atoll of Aldabra provides a unique opportunity to study evolution and biological process because of its undisturbed nature^{1,2}. Interpretations of the geomorphology by Stoddart *et al.*³ have now been superseded by a detailed geological survey in 1969 by Braithwaite, Kennedy and Taylor (manuscript in preparation), who discovered a complex stratigraphy involving both marine and terrestrial deposits. Most of the present land area, however, is formed from two extensive marine deposits. The lower and older of these consist largely of a fine calcarenite characterized by abundant calcareous red algae, but with few corals and molluscs. Most originally aragonitic skeletons are recrystallized. The deposit rises to about 2 m. above present sea level, and is separated by an erosion surface and sometimes terrestrial deposits from an extensive upper limestone consisting of coarse calcarenites to calcrudites with abundant well preserved corals and molluscs. This deposit occupies most of the outer rim of the atoll and rises to around 8 m. above present sea level. Subsequent marine erosion has cut an ill-defined terrace at 8 m and a well-marked one at 4 m.

Radiocarbon ages of mollusc shells from the upper coral-rich limestone were reported by Stoddart *et al.*³. These samples yielded dates from 26.95 to more than 39.9 kyr, with most between 34 and 39 kyr. Such ages may be produced by contamination of an infinitely old sample (> 39.9 kyr) with only a few per cent of natural modern carbon. Accordingly, we have determined ages for seven coral samples from various localities in the upper coral-rich limestone by the ²³⁰Th/²³⁴U method.

The coral samples, most of which had been exposed recently by cliff falls, were collected from their positions of growth on

Fig. 1 Map of Aldabra Atoll ($9^{\circ} 24' S$, $46^{\circ} 20' E$) showing sampled localities. The numbers correspond to samples listed in Table 1.



Aldabra Atoll. All weathered or discoloured surfaces were sliced off, and the fresh coral then crushed. Chemical procedures have been described elsewhere⁴. Briefly, about 10 g of coral was dissolved and spiked with a calibrated ^{232}U - ^{228}Th solution at radioactive equilibrium. Uranium and thorium isotopes were separated by solvent extraction and ion exchange, and the purified fractions mounted on stainless steel disks from TTA-benzene solutions. Alpha spectrometric analyses were performed using two 300 mm² silicon surface barrier detectors and a 400 channel analyser. The Mississippi Spargen Limestone standard samples, which are old enough for secular equilibrium to have been achieved, indicate no systematic error in the analyses (Table 1).

Table 1 Analytical Data on Coral Samples

Sample No.	Species	Aragonite %	U (p.p.m.)	$(^{234}U/^{238}U)^{\dagger}$	$(^{230}Th/^{234}U)^{\dagger}$	Age ($\times 10^{-3}$ yr)
1*	<i>A. palifera</i>	100	3.59	1.09 ± 0.01	0.70 ± 0.02	126 ± 8
2*	<i>A. palifera</i>	100	3.55	1.11 ± 0.01	0.69 ± 0.02	123 ± 8
3	<i>Goniastrea</i> sp	100	2.48	1.10 ± 0.01	0.72 ± 0.02	136 ± 9
4	<i>P. nigrescens</i>	100	3.40	1.09 ± 0.01	0.66 ± 0.02	118 ± 7
5	<i>Porites</i> sp	100	2.60	1.10 ± 0.01	0.73 ± 0.02	136 ± 9
6	<i>Porites</i> sp	100	3.13	1.11 ± 0.01	0.72 ± 0.02	134 ± 9
7	<i>A. palifera</i>	100	3.09	1.10 ± 0.01	0.73 ± 0.02	136 ± 9
8	<i>Porites</i> sp	100	2.82	1.13 ± 0.01	0.69 ± 0.02	124 ± 8
9†	<i>Porites</i> sp	< 10	1.19	1.02 ± 0.02	1.04 ± 0.04	
MSL§			$\begin{cases} 1.07 \\ 1.10 \end{cases}$	$\begin{cases} 1.01 \pm 0.01 \\ 1.01 \pm 0.01 \end{cases}$	$\begin{cases} 1.03 \pm 0.02 \\ 1.02 \pm 0.02 \end{cases}$	

* Samples 1 and 2 are from the same large coral head. *A. palifera*, *Acropora palifera*; *P. nigrescens*, *Porites nigrescens*.

† Activity ratio.

‡ Sample from the lower algal-rich limestone.

§ Mississippi Spargen Limestone.

Our data (Table 1) show that the upper limestone samples satisfy the criteria established by Thurber *et al.*⁵ for reliable $^{230}Th/^{234}U$ ages on corals: (1) The samples contain no calcite above the limit of detection (0.5%) which indicates that no recrystallization of the original aragonite has occurred. (2) The uranium concentrations are between 2.6 and 3.6 p.p.m., which compares with previously determined coral values between 2.0 and 4.0 p.p.m. (Moore, W. S., Krishnaswamy, S., and Bhat, S. G., preprint). (3) No ^{232}Th was detected in any of the samples, indicating that thorium isotope contamination since formation is improbable. (4) The $^{234}U/^{238}U$ activity ratios, when corrected for age, lie in the range 1.15 ± 0.03 , the sea water value.

Sample ages were calculated by the equation derived by Broecker⁶, using half lives of 75.2 kyr and 248 kyr for ^{230}Th and ^{234}U respectively. The ages thus obtained for the upper limestone are in the range 127 ± 9 kyr, and the uncertainty is similar to the error on each determination as derived from one σ counting uncertainties.

The consensus of $^{230}Th/^{234}U$ dating indicates that the last time sea level stood higher than it does today was at the beginning of the last interglacial, circa 125 kyr BP, at 2 to 4 m higher than present sea level⁷⁻⁹. It is uncertain how long this high sea stand persisted, although Veeh and Chappell¹⁰ have suggested between 118 and 140 kyr BP.

We correlate the Aldabra upper marine limestone with this last interglacial high sea level stand. The geological evidence suggests that relative sea level stood at least 8 m above the present. Although tectonic uplift cannot be discounted, the occurrence of corals at 6 to 9 m around the granitic Seychelles, dated by Veeh¹¹ at 140 ± 30 kyr, tends to support a general stability of the area in the late Pleistocene. The high stand at 8 m would thus appear to be real.

Unfortunately, no dates are available for the lower, older algal-rich limestone. The best available sample (Table 1) failed to satisfy the criteria for reliable dating, but samples from boreholes may be sufficiently unaltered to extend the dated sequence further back into the Pleistocene. This is important since geological evidence has indicated at least two major inundations of the Atoll (one at 125 kyr BP) which would have eliminated the contemporary terrestrial biota. This means that the present flora and fauna, including the giant tortoise, have colonized the Atoll within the last 125 kyr. Further dating of older samples could provide us with important information on the rates of colonization and extinction of an oceanic island.

We thank Drs W. J. Kennedy and J. D. Taylor for coral samples and for discussions.

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The So-called Thermodynamic Compensation Law and Thermal Death

It has frequently been reported that, for a structurally related series of compounds undergoing a defined chemical reaction, the activation parameters, $\Delta H^\ddagger$ and $\Delta S^\ddagger$, are linearly related:

$$\Delta S^\ddagger = a\Delta H^\ddagger + b \quad (1)$$

This is sometimes called a thermodynamic compensation law because the form of the rate equation derived from transition state theory (equation (2)) is such that parallel changes in the activation parameters have opposite effects on the value of the rate coefficient, k ,

$$\log k - \log \frac{KT}{h} = \frac{\Delta S^\ddagger}{2.303 R} - \frac{\Delta H^\ddagger}{2.303 RT} \quad (2)$$

As Leffler¹ pointed out, however, the relationship can arise as a computational artefact from experimental errors in the rate coefficients from which the activation parameters are calculated. Exner^{2,3} further showed that the form of the equations used in the calculation tended, in any case, to generate the relationship. Hammett⁴, from statistical mechanical considerations, has produced a set of formal conditions which must be satisfied if the relationship is to be observed but these seem to have no simple physical interpretation. Behaviour which appears to be consistent with the compensation law makes a comparison of rate constants of doubtful value since, at a temperature $T=1/a$, all the rate coefficients are the same. Above this so-called isokinetic temperature the order of rate coefficients is the reverse of that observed below it (see ref. 5).

Recently, the relationship has been claimed to apply to the denaturation of proteins^{6,7} and to the thermal killing of yeasts, bacteria and viruses⁷. It has been argued⁷ that because the compensation law constants (a and b in equation (1)) are virtually the same for all these processes ($1/a=325\text{--}331\text{ K}$, $b=-64$ to $-65\text{ cal mol}^{-1}\text{ deg K}^{-1}$) one may conclude that "protein denaturation is the cause of thermal death in unicellular organisms". Graphs presented by these authors suggest that the compensation law is obeyed with extraordinary precision. We suggest that this apparent behaviour is wholly artefactual.

In physical organic chemistry, values of $\Delta H^\ddagger$ are usually in the range $15\text{--}30\text{ kcal mol}^{-1}$, whereas for protein denaturation and the thermal death of unicellular organisms the ranges of values are much wider ($10\text{--}140\text{ kcal mol}^{-1}$ and $25\text{--}200\text{ kcal mol}^{-1}$ respectively). It is difficult to imagine any unit step, occurring at ordinary temperatures, having a value of $\Delta H^\ddagger$ of 150 kcal mol^{-1} because such a process, if associated with a "normal" value for $\Delta S^\ddagger$ (-20 to $+20\text{ cal mol}^{-1}\text{ deg K}^{-1}$), would escape detection by present observational methods, the half life being about 10^{50} yr . Such large values of $\Delta H^\ddagger$ must be associated with complex processes, individual chemical events taking place in sequence. The resulting apparent $\Delta H^\ddagger$ may then be large, if the $\Delta H^\ddagger$ values for individual steps are largely added, or small or even negative if largely subtracted (our unpublished results).

The greatest objection to the conclusions drawn in ref. 7 is as follows. The experimental data consist of rate measurements, carried out as a series of temperatures. The usual plot of the logarithm of the rate coefficients against the reciprocals of absolute temperature then enables $\Delta H^\ddagger$ to be calculated. Substitution of $\Delta H^\ddagger$ into equation (2) then gives $\Delta S^\ddagger$. T is normally in the range $295\text{--}345\text{ K}$ for the processes under discussion, and the term $\log KT/h$ will, therefore, be approximately constant, with a value of about 13. The values of the rate coefficients, k , will usually be in the range 10^{-3} to 10^{-6} s^{-1} , corresponding to half-lives of about 10 min and 7 days respectively (any kineticist will adjust his rates, by change of temperature, so that they fall inside this range, otherwise

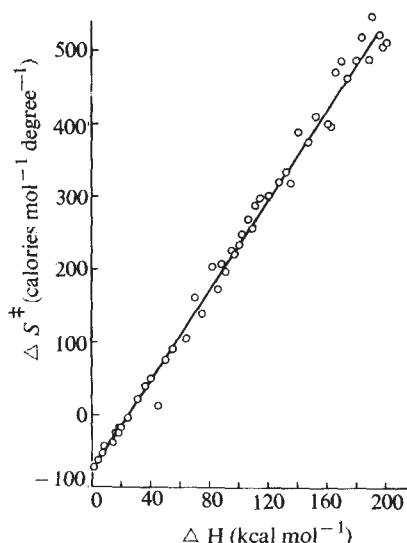


Fig. 1 Arbitrary values of rate coefficients plotted against $\Delta S^\ddagger$, calculated from equation (2).

the reactions will be inconveniently fast or inconveniently slow). This means that the left hand side of equation (2) varies between -16 and -19 , so it is roughly constant. This approximate constancy arises partly from the logarithmic form of the left hand side of the equation and partly because the temperature range is so narrow and the range of observed reaction rates is limited. The quantities on the right hand side of equation (2) are, on the other hand, not in logarithmic form. With values of $\Delta H^\ddagger$ varying between 10 and 200 kcal mol^{-1} , the quantity $-\Delta H^\ddagger/2.303 RT$ will vary between -7 and -135 , that is, about twenty-fold, while the variation in the left hand quantity is only about 20%. It follows that $\Delta S^\ddagger/2.303 R$ must change by approximately the same amount as $\Delta H^\ddagger/2.303 RT$ in the opposite direction. Hence the compensation law.

Fifty arbitrarily selected hypothetical values of rate coefficients between 10^{-3} and 10^{-6} s^{-1} , temperatures between 295 and 345 K and apparent enthalpies of activation between 10 and 200 kcal mol^{-1} were randomly associated and the corresponding values of $\Delta S^\ddagger$ calculated from equation (2). The results are plotted as $\Delta S^\ddagger$ against $\Delta H^\ddagger$ (Fig. 1) and it is clear that the graph could be taken as representing compensation-law behaviour. The characteristics of the best straight line (calculated by least squares) are $1/a=322\text{ K}$ (the apparent isokinetic temperature), $b=-77.7$. These values are close to those quoted in reference 7. However, it should be noted that the value of $1/a$ is merely the mean of the arbitrarily chosen temperatures (320 for the 50 values taken for the graph) while b is determined by the mean value of the left hand side of equation (2) (-76.3 for the data illustrated in the graph). Because the apparently linear relation between $\Delta H^\ddagger$ and $\Delta S^\ddagger$ in the figure is not associated with any physical process it can have no physical significance.

The type of treatment under discussion may not be applied to complex processes because the equation is inappropriate. The derivation of equation (2) is based on a number of assumptions which may, though there are difficulties, be justified for simple reactions occurring in the gas phase. Useful results may then be obtained. In the condensed phase, however, even for simple reactions, the situation is less clear and the significance of the activation parameters becomes doubtful. Entirely unrelated processes may give data falling on a single graph of $\Delta S^\ddagger$ against $\Delta H^\ddagger$ given only that the temperature range over which the processes occur is the same in all cases and that rate constants fall within the specified range.

It may be noted, in passing, that the fact that the processes under discussion are kinetically first order is also not particu-

arly significant, since, if one distinguishes between two kinds of bacterial cell, dead and alive, death is necessarily first order. This is true, as for radioactive decay, irrespective of mechanism.

Two of us (B. E. C. B. and C. A. V.) wish to thank the authorities of SNAM PROGETTI (Milan) for hospitality enjoyed in the Laboratories at Monterotondo during which time they became interested in temperature effects on complex processes.

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BIOLOGICAL SCIENCES

Platelet Shape Change and Aggregation

A PREVIOUSLY described¹ modification of the optical method of Born allows the simultaneous measurement of scattered and transmitted light during the course of action of different inducers and inhibitors of platelet aggregation. Using this

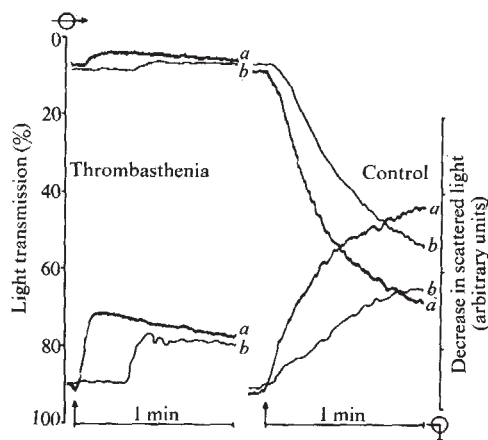


Fig. 1 Ten μ l. adenosine ($50 \mu\text{M}$ concentration) was added to 1.0 ml. of citrated control or thrombasthenic PRP (platelets $300,000 \text{ mm}^{-3}$), incubated and stirred for 2 min before the addition of the aggregating agent $\uparrow$ (ADP- $10 \mu\text{M}$ final concentration). Light transmission $\rightarrow$ change (%) and decrease in scattered light (in arbitrary units) $\rightarrow$ are then recorded simultaneously during a 1 min period. a, ADP; b, ADP with adenosine.

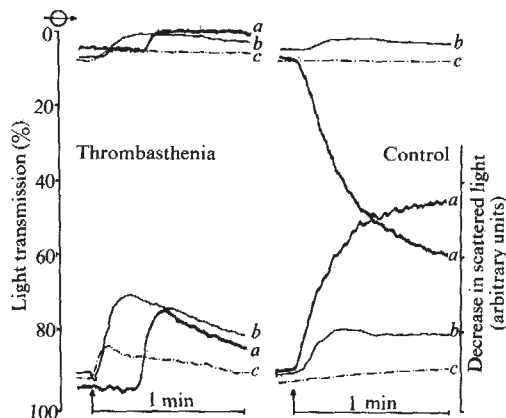


Fig. 2 To 0.9 ml. of citrated control or thrombasthenic PRP (platelets $300,000 \text{ mm}^{-3}$) plus 0.1 ml. veronal acetate buffer, pH 7.4 (a) or EDTA (b) (2 mM final concentration), 10 μ l. buffer (b) or adenosine ($50 \mu\text{M}$ final concentration) (c) was added, incubated and stirred for 2 min before the addition of the aggregating agent $\uparrow$ (ADP- $3 \mu\text{M}$ final concentration). Light transmission change and decrease in scattered light estimated as in Fig. 1.

technique we have distinguished the shape change from platelet aggregation, using thrombasthenic platelets, which are unable to aggregate in the presence of adenosine diphosphate (ADP) or purified calf-skin collagen². These platelets respond to bovine fibrinogen³ and one of our objectives was to establish whether this latter compound allowed the shape change of thrombasthenic or normal platelets.

The cuvette chamber of the aggregometer was used as described by Michal and Born¹ stirred magnetically at 1,150 r.p.m. Human citrated platelet-rich plasma (PRP) was prepared as described elsewhere (1 volume 3.8% citrate to 9 volumes of blood)³. Experiments were carried out using 1 ml. 250,000 platelets/cu mm in citrated plasma, 10 μ l. aggregating agents and 10 μ l. inhibitor. The mixture (PRP with or without adenosine or EDTA as inhibitor) was incubated and stirred for 2 min to reach temperature equilibrium (37°C) before addition of the aggregating agent. The aggregometer tube was shielded to reduce illumination. 10 μ l. aggregating agent (ADP, pre-polymerized purified calf-skin collagen² or bovine fibrinogen) was injected through a microsyringe needle inserted through the small hole in the cap.

Fig. 1 shows that for the control sample there is a relationship, during the 1 min after addition of ADP, between the change in optical transmission and the decrease in scattered light in the presence of ADP and the presence or absence of adenosine. With thrombasthenic PRP there is no optical density transmission (no aggregation) while adenosine ($50 \mu\text{M}$) preincubated for 2 min appears to delay the fast initial response of the scattering of the light induced by ADP ($5 \mu\text{M}$).

A given dose of EDTA (2 mM) (Fig. 2) completely inhibits platelet aggregation but does not completely prevent the change in shape of the control sample⁵; the same dose appears to increase the change in shape of the thrombasthenic platelets without any lag period obtained with ADP alone. Adenosine in the presence of EDTA inhibited the shape change and platelet aggregation of the control sample and partly reduced the change in shape with thrombasthenic platelets (Fig. 2) which lack the surface platelet contractile protein⁶. Also, using control PRP and purified calf-skin collagen, we found a lag phase period before light transmission change as well with decrease in scattered light. Using EDTA we have shown complete inhibition of the light transmission and of scattered light, while with thrombasthenic PRP, EDTA inhibits the rate at which the changes occur but not the total loss of light scattering (Fig. 3) in the presence of collagen.

Purified bovine fibrinogen³ does not induce reduction in light scattering for control or thrombasthenic platelets in PRP;

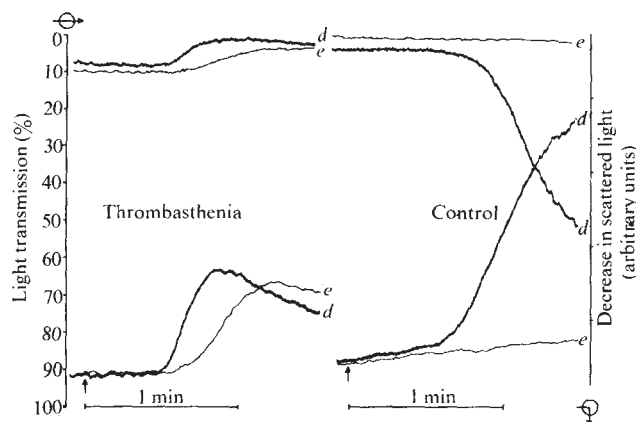


Fig. 3 Light transmission change $\rightarrow$ and decrease in scattered light $\rightarrow$ are recorded simultaneously for 0.9 ml. control or thrombasthenic citrated PRP in the presence of 0.1 ml. buffer (d) or EDTA (2 mM final concentration) (e) and purified calf skin collagen (1.6 μ g final concentration).

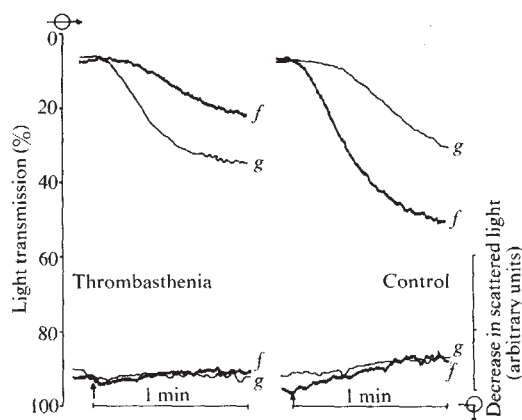


Fig. 4 Light transmission change $\rightarrow$ and decrease in scattered light $\rightarrow$ are recorded simultaneously for 0.9 ml. control or thrombasthenic citrated PRP in the presence of 0.1 ml. buffer (f) or EDTA (2 mM final concentration) (g) and bovine fibrinogen (0.32 mg final concentration).

its activity on light transmission is decreased by EDTA with control platelets but is increased with thrombasthenic PRP (Fig. 4).

The primary step of haemostasis is the collagen platelet reaction⁷, in which the role of collagen glucosyl transferase is important. Our experiments suggest that platelet : collagen interaction is normal in thrombasthenia as far as the shape change is concerned. The collagen-induced shape change in thrombasthenia is increased by EDTA but partially inhibited and delayed by adenosine. The nucleotide release by collagen is normal in thrombasthenia⁷ and we postulate that 4 stages in platelet-collagen interactions exist. These stages are: 1, Platelet adhesion to collagen (platelet shape change) which is normal in thrombasthenia. 2, Platelet shape change with ADP which is also normal in thrombasthenia. 3, Platelet aggregation, subsequent to shape change, which is abnormal and of an unknown origin but may possibly be related to a decrease of surface contractile protein⁶ or an increase in I-fucose⁸. 4, The release phenomenon which is normal in thrombasthenia. We were also able to show that the bovine fibrinogen induced platelet agglomeration intervenes without shape change and that this agglomeration (light transmission change) is increased by EDTA in thrombasthenia.

We tentatively suggest that a transferase, different from the glucosyl transferase, is abnormal in thrombasthenic platelet

membranes and can account for the abnormal ADP or collagen-induced aggregation.

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Chromosomal Localization of Human Haemoglobin Structural Genes

PRICE *et al.*¹ recently claimed to have located the structural genes for haemoglobin on human chromosomes 2 and 4 or 5 by *in situ* hybridization using labelled haemoglobin mRNA. We wish to warn against a too ready acceptance of their conclusion.

The specific radioactivity of the mRNA used is given as 6 disintegrations/2 weeks/10 molecules of molecular weight 200,000. This is very close to 100 d.p.m./ μ g. If we assume that roughly 10% of all disintegrations generate silver grains², one grain will be produced on average by 3×10^{12} daltons of mRNA. In the regions of interest (chromosomes 2 and 4 or 5) approximately seventy silver grains were found, corresponding then to about 2×10^{14} daltons of mRNA. These grains were observed amongst approximately 1,000 metaphase karyotypes, each of which contains 4C chromosomes or 7.2×10^{12} daltons of DNA³. In effect about 7×10^{15} daltons of DNA were examined for the presence of grains. Thus, if it is indeed hybridization of mRNA that is being observed, we can calculate that 1 part of DNA hybridized with about 0.025 parts of mRNA. In other words, if the efficiency of *in situ* hybridization is 100%, the haemoglobin genes must make up about 5% of the total genome. If, as we believe, the efficiency is much less⁴ the proportion of the genome made up by haemoglobin genes would be yet higher.

It is, of course, unlikely that a single gene makes up even 5% of the human genome. Furthermore, there is direct evidence that both in the duck (ref. 5 and unpublished experiments of J. O. B. and M. Rosbash) and the mouse (Harrison *et al.*, unpublished work) the reiteration frequency of the haemoglobin genes is very low, certainly less than five. In contrast the 5% figure would mean a reiteration frequency on the order of 10^5 in man.

In RNA excess hybridization experiments haemoglobin mRNA preparations saturated 0.5% and 2.5% of mouse⁶ and chicken⁷ DNA. The mouse hybrid was found to have a low thermal stability, indicating a high level of mis-matched base-pairs⁶ and its formation was largely inhibited by homopolyribonucleotides, such as poly-(A) or poly-(U)⁸. Evidently this is a relatively non-specific hybrid which may or may not involve a part of the haemoglobin mRNA.

In situ hybridization is an RNA-excess hybridization technique, and is open to the same weakness, that when a heterogeneous mixture of RNA molecules is used the sequences which

react may not be representative of the RNA as a whole. We wish to emphasize that in such cases it is important to establish, or at least to attempt to establish, the identity of the hybrids.

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Drs Price, Conover and Hirschhorn write: Bishop and Jones raise doubts about our suggested localization of human haemoglobin genes on chromosomes 2 and 4 or 5¹. We agree in general with their abstract calculations, although there appear to be at least seven or eight haemoglobin genes in man (two or three alpha, two gamma, one beta, one epsilon)⁹. Also, their comments on non-specific hybridization with RNA excess refer to experiments using isolated DNA, and not *in situ* metaphase chromosomes. It is, of course, not feasible at this time to establish the identity of hybrids produced in this manner.

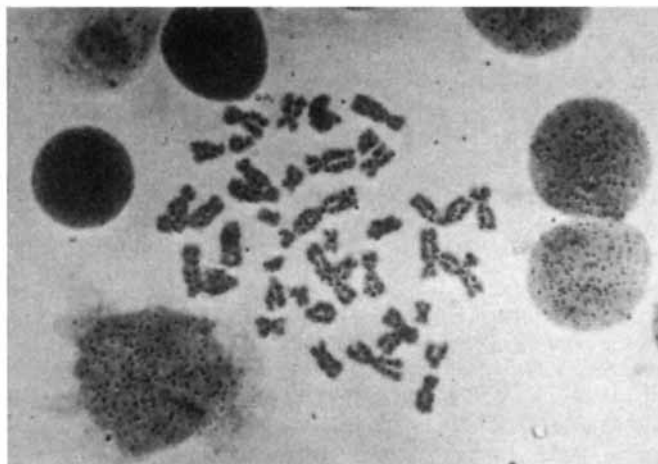


Fig. 1 Autoradiograph of human metaphase chromosomes and nuclei; emulsion exposed for 2 weeks. Labelling produced by hybridization¹ with RNA labelled with ³H-uridine in transformed fibroblast cultures and collected as the ethanol-precipitable nucleic acid after phenol extraction. Note the high, diffuse labelling of chromosomes and nuclei with almost complete absence of background.

We cannot, however, accept their general criticism, since they completely ignore the critical findings leading to our conclusion. This is the fact that radioactivity was found only in two small highly restricted chromosomal regions, which are certainly far less than 5% of the total genome. Nonspecific hybridization would be expected to show more diffuse labelling (Fig. 1). Instead, their criticism stems from calculations based on our somewhat irrelevant estimate of specific activity, in itself derived from several assumptions and approximations.

Since we cannot reconcile their calculations to our findings, and they cannot explain our specific localization, it is possible that the assumptions inherent in the calculations do not apply to our experimental technique. The final verdict will have to await verification of our gene assignment by appropriate genetic linkage data or family studies on families with relevant chromosomal rearrangements.

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Characterization of Heinz Bodies in Unstable Haemoglobin Haemolytic Anaemia

THE unstable haemoglobins are a group of well-defined haemoglobin variants associated clinically with haemolytic anaemia of varying severity^{1,2}. The nature of the amino-acid substitutions reduces the stability of the haemoglobin molecule, and this results in precipitation within the red cell and formation of characteristic inclusions called Heinz bodies. The instability of this group of haemoglobins is also shown by their precipitation from solution when subjected to mild heating. The cellular inclusion bodies are generally not present unless the patient has been splenectomized, but can usually be induced by incubating the blood at 37° C for up to 48 h. Although it is generally accepted that the Heinz bodies consist of denaturation products of the abnormal Hb, as yet they have not been analysed directly, and there is some speculation as to their actual constitution²⁻⁴. In particular, it has been postulated that only the abnormal chains of the tetrameric Hb molecule precipitate, and that these may be lacking haem groups⁴. Some work has been done on the inclusion bodies which occur in the thalassaemias, in which there is impaired production of one of the polypeptide chains. Fessas *et al.*⁵ have shown that in β -thalassaemia, the peptide map of the inclusion bodies closely resembles that of pure α chains, and Rachmilewitz *et al.*⁶ have shown that in Hb H disease (α -thalassaemia) the inclusions are primarily β -chains largely present as haemichromes.

We have separated Heinz bodies from a patient whose red cells contain Hb Christchurch $\beta 71$ Phe $\rightarrow$ Ser and shown by peptide mapping of the solubilized protein that they contain only the abnormal Hb and that α - and β -chains are present in approximately equal amounts. Our examination of heat precipitates of several unstable Hbs has also shown the presence of equivalent proportions of α - and β -chains.

Red cells for Heinz body examination were obtained from a patient with a typical unstable haemoglobin haemolytic anaemia associated with the presence of about 20% Hb Christchurch⁷. She has been splenectomized and her circulating red cells contain an average of 30 Heinz bodies per hundred cells. We examined fresh cells and cells which had been incubated for 48 h at 37° C under sterile conditions. These cells contained an average of 48 larger than normal Heinz bodies per hundred cells, and also some material deposited around the cell periphery which stained like Heinz bodies, but lacked the typical Heinz body shape.

Red cell ghosts were prepared by haemolysis in hypotonic phosphate buffers by the method of Dodge *et al.*⁸. Whereas normal red cells yielded opaque white ghosts, those obtained from cells containing Hb Christchurch were light brown, and those from the incubated cells were dark brown. Ghosts from the fresh cells, stained with methyl violet, appeared normal microscopically, but with numerous typical Heinz bodies attached to the membranes (Fig. 1). Ghosts from the incubated cells were similar, with a greater number of larger, membrane-bound Heinz bodies. More stain had been taken up at the

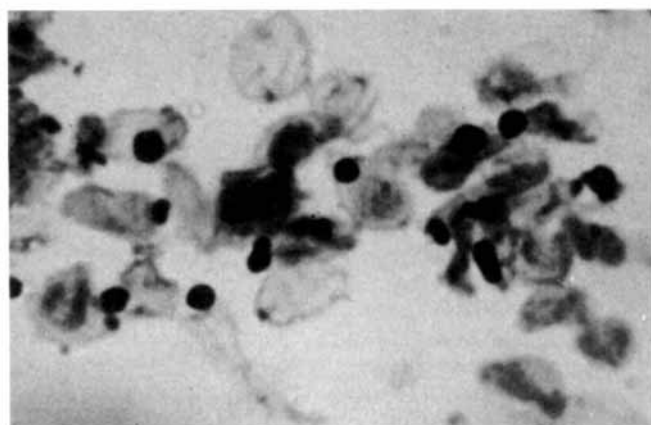


Fig. 1 Micrograph of red cell ghosts containing Heinz bodies from splenectomized patient with Hb Christchurch disease. Methyl violet stain.

periphery of these ghosts, indicating the presence of further precipitated Hb at the membrane surface.

Heinz body material was separated from ghost proteins by column chromatography on 'Sephadex G200' in pH 6.8 citrate buffer in the presence of 0.2% SDS. The ghosts and Heinz bodies were first solubilized at pH 8 in 3% SDS containing 1% mercaptoethanol. A preliminary experiment using polyacrylamide gel electrophoresis in the presence of SDS had shown that the solution contained normal ghost proteins, all with molecular weights greater than 30,000, and in addition, a clearly separated band which ran in the same position as the polypeptide chains of haemoglobin, molecular weight about 17,000. This fast band was the only protein to stain significantly with the haem-specific *o*-toluidine stain. It was possible to separate this low molecular weight component on 'Sephadex G200'. The protein was purified from both fresh and incubated red cells, and peptide maps were prepared after precipitation with acid acetone and digestion with trypsin⁹. Fig. 2 shows a peptide map of the Heinz body protein from the incubated red cells.

The protein is almost entirely Hb Christchurch, as evidenced by the presence of the abnormal β IX and β VIII-IX peptides, although small amounts of the normal peptides from Hb A are just detectable. Heinz bodies from the fresh cells produced essentially the same pattern, except that only Hb Christchurch was detectable. In the extended period during which the cells in the first sample were incubated a small amount of precipitation of normal Hb could be expected. Apart from the two abnormal peptides, these peptide maps are visually indistinguishable from a peptide map of Hb A. Both α and β -chain peptides are present in similar yields, suggesting that the Heinz bodies consist of equal quantities of both chains of the unstable

Hb. A quantitative measure of the relative amounts of α and β chains was also made by amino-acid analysis of the two Heinz body preparations (Table 1). They suggest that the Heinz bodies contain similar amounts of the two chains, with perhaps a slight excess of the β -chain, although this is within the range of the inherent variability of quantitative amino-acid analysis.

Table 1 Proportions of α - and β -Chains in Heinz Bodies and Heat Precipitates

		Mean percentage	
		α -chains	β -chains
Hb Christchurch	Heinz bodies from fresh cells	43	57*
	Heinz bodies from incubated cells	42	58†
	Heat precipitate	48	52‡
		48	52‡
		52	48‡
Hb Sydney		50	50‡
	Heat precipitate	51	49‡
		40	60‡

Percentages were determined by quantitative amino-acid analysis.

* From the ratio of alanine to glycine in tryptic peptide α - β VII. The α and β peptides differ only in one alanine and glycine, and are not separated by peptide mapping.

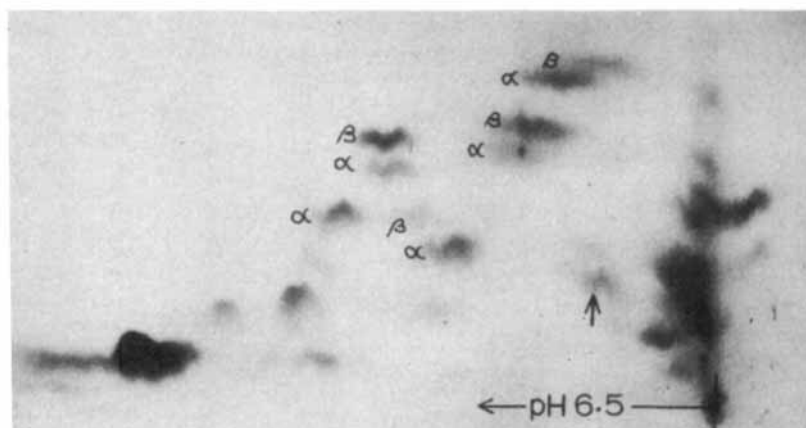
† From the number of glycine, serine and glutamic acid residues in a hydrolysate of the total protein.

‡ From the number of glycine, serine, glutamic acid and cysteic acid residues in a total protein hydrolysate after performic acid oxidation.

In addition to analysis of Hb Christchurch Heinz bodies, we have also examined heat precipitates of several unstable Hbs for their subunit composition. We used heat precipitation at 50° C as a standard method for purification of unstable Hbs and examined peptide maps of heat precipitated Hb Köln β 98 Val→Met, Hb Hammersmith β 42 Phe→Ser, Hb Sydney β 67 Val→Ala and Hb Christchurch. In each case the peptide map showed the presence of the abnormal β -chain, with an apparently equal amount of the coprecipitated α -chain. Quantitative amino-acid analyses were performed on heat precipitates of Hb Christchurch and Hb Sydney, to determine the proportions of α - and β -chains present. The results, shown in Table 1, are further support for the conclusion that the whole protein is precipitated. This is also substantiated by our unpublished findings that there is no accumulation of soluble α -chains during heat precipitation of Hb Christchurch. Contrary to other reported results^{2,4}, we found that the small amount of free α -chains, that can be detected in fresh haemolysates by starch gel electrophoresis, quickly disappeared on heating at 50° C, and at no later stage were α -chains detectable.

We have not measured the haem content of Heinz bodies directly but other evidence suggests that the unstable Hbs we have studied precipitate intact. The brown colour of ghost

Fig. 2 Peptide map of tryptic digest of Heinz bodies separated from ghosts of incubated red cells containing Hb Christchurch. α and β peptides (marked) are present in similar proportions to those in standard peptide maps of Hb A. The β chain present is almost entirely from Hb Christchurch as shown by the abnormal peptide β VIII-IX (arrowed).



preparations containing Heinz bodies infers the presence of haem groups, and we have also measured haem:globin ratios in heat precipitates of Hb Christchurch and Hb Sydney and in each case found the theoretical number of four haems per tetramer.

The unstable Hbs we have examined form precipitates intracellularly or on mild heating which contain haem groups and both α - and β -chains. However, mechanisms of Heinz body formation have been proposed in which only the abnormal chain of the unstable haemoglobin precipitates, having first released its haem groups²⁻⁴. Although we cannot deny the possibility of this occurring in isolated instances our results are contrary to this being a general mechanism of Heinz body formation from unstable Hbs.

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Studies in Ageing

Holliday and Tarrant¹ appear to have ignored studies on ageing in ciliated protozoa, as has editorial comment on this work². Senescence is one of the most widely investigated and longstanding problems of protozoan genetics³. The contribution of nuclear and cytoplasmic changes has been recognized and cogent arguments have been presented for progressive nuclear changes⁴ and for random cellular accidents⁵ as the basis for ageing. The ciliated protozoa possess a compound macronucleus, and therefore have a high degree of gene duplication, but age, as do other organisms, and with quite variable lengths of life cycle times.

I do not want to detract in any way from the contribution of Holliday and Tarrant, but I would like to make a plea that as biologists begin to study ageing in tissue culture and other biological systems, they become aware of such studies that have already been carried out in protozoan systems, and which may help shed some light on this very basic biological problem.

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Do the *H-2* and *T*-Loci of the Mouse have a Function in the Haploid Phase of Sperm?

It is still uncertain whether there is any gene activity in the haploid phase of mammalian sperm¹, after meiosis in the maturing spermatids and spermatozoa. Two loci at which haploid activity possibly occurs in the mouse are the *H-2* antigen locus and the *T* or brachyury locus, both situated near the centromeric end of chromosome 17 (linkage group IX)². Evidence that the *T*-locus may act in the haploid phase comes from the effect of some alleles in distorting segregation ratios in the male^{3,4}. Males heterozygous for certain recessive alleles give a very high proportion (up to 99%) of *t*-carrying young. Other alleles give an abnormally low proportion of young with the *t*-allele (10–20%) and yet others give a normal 1:1 ratio of + : *t*-carrying offspring. Although the mechanism of this effect is unknown it may well involve some action of the *t*-alleles concerned at the haploid stage. Antigens of the *H-2* locus are expressed on mouse spermatozoa⁵. It has been claimed that both the human HL-A antigens and the mouse *H-2* antigens on spermatozoa are produced by gene action at the haploid stage⁶, but for *H-2* other authors have expressed doubt⁷.

If *H-2* antigens are produced at the post-meiotic stage and are essential to fertilization, then sperm lacking the relevant region of chromosome 17 should be unable to fertilize; similarly, if the *t*-locus has some haploid action, such that some mutational changes can distort the segregation ratio, then total absence of the locus might prevent fertilization entirely.

We can test this by reciprocal translocations. Heterozygotes for such translocations produce "unbalanced gametes" with duplications and deficiencies of the translocated regions. If an unbalanced gamete unites with a balanced gamete from the other parent then the zygote is inviable, but if two unbalanced gametes with complementary deficiencies and duplications unite then a viable offspring may result. If offspring formed in this way can be found, they constitute evidence that the unbalanced gametes were capable of fertilization. Snell⁸ and more recently Searle *et al.*⁹ showed that such offspring can be recognized, in appropriate mouse crosses, because they carry two recessive alleles from the same parent and none from the other. It is possible to obtain *cc* offspring from a cross of *cc* by + +^c. If the marker gene is located between the translocation break and the centromere, such homozygous offspring can only occur as a result of adjacent-2 disjunction (in which homologous centromeres pass to the same pole).

A reciprocal translocation involving chromosome 17 is *T*(9;17)138 Ca. The translocation break in chromosome 17 is distal to both the *T* and *H-2* loci and that in chromosome 9 (linkage group II) is distal to the locus of curly whiskers, *cw*^{2,10-12}. As part of a study of adjacent-2 disjunction in this translocation, *T*138 heterozygotes marked with two *T*-locus alleles (*T* and *t*^{h2}) were mated to those wild-type for *T* but marked with the chromosome 9 gene *cw* (Fig. 1). Genetically *T*+ animals are short-tailed, +*t*^{h2} are normal-tailed and *Tt*^{h2} are tailless. The allele *t*^{h2} was chosen as it was a *t*-allele not known to distort segregation ratio nor to affect crossing-over in its region (another effect of some *t*-alleles)¹³. With normal disjunction all offspring would be + *cw* and either *T*+ (short-tailed) or +*t*^{h2} (normal-tailed). Adjacent-2 disjunction would give, among others, unbalanced gametes carrying both *T* and *t*^{h2} from one parent and those with no *T*-alleles but with two *cw* alleles from the other. Union of two such gametes would give a chromosomally balanced and potentially viable zygote, genotypically *Tt*^{h2} *cwcw* and phenotypically tailless and curly whiskered.

From crosses in which the mother carried *Tt*^{h2} and the father *cwcw* there were 23 *Tt*^{h2} *cwcw* offspring. Reference to Fig. 1 shows that these must have received a male gamete lacking that part of chromosome 17 carrying the *T* and the *H-2* loci. This shows

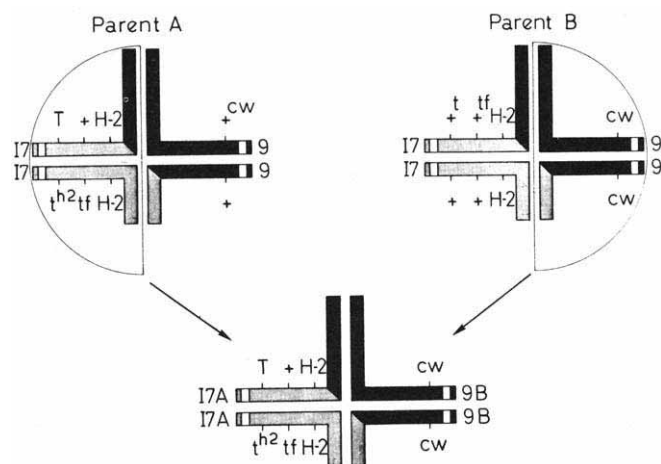


Fig. 1 Diagrammatic representation of the configurations at meiosis of the heterozygous $T138/+$ animals used in the test crosses, and the mechanism by which the phenotypically tailless curly-whiskered offspring ($Tt^{h2} cwcw$) were presumed to have arisen. By adjacent-2 disjunction two chromosome 17 centromeres were contributed by one parent and two chromosome 9 centromeres by the other. Not to scale.

conclusively that neither of these gene loci has a haploid action essential to fertilization. However, it does not rule out the possibility that they do have a haploid expression not required for fertilization.

Table 1 Frequency of Offspring from Adjacent-2 Disjunction among Progeny of Pairs of $T138/+$ Heterozygous Mice, Carrying Marker Genes in Interstitial Segments

♀	Parents		♂	Offspring		Adjacent-2 %
	Tt^{h2}	$++^{cw}$	$++^{t}$	T or $cwcw$	Tt^{h2}	
Tt^{h2}	$++^{cw}$	$++^{t}$	$cwcw$	590	1*	23
$++^{t}$	$cwcw$	Tt^{h2}	$++^{cw}$	703	2*	2

* The explanation for the single $cwcw$ animal and the two Tt^{h2} non- cw is not known. They could have arisen through numerical non-disjunction, crossing-over between the T -locus and centromere ($cwcw$ animal only) or through misclassification of $T+$ as Tt^{h2} (Tt^{h2} animals only). However, all three died or became sterile before genetic tests were completed.

An intriguing observation is that the frequency of $Tt^{h2} cwcw$ offspring was much lower after the reciprocal cross, with the mother carrying $cwcw$ and the father Tt^{h2} (Table 1). The reasons for this are not clear. As at least some non-disjunctional offspring were obtained from both types of cross, all the various relevant types of unbalanced gamete must be capable of fertilization, including male gametes with duplication of the relevant segment of chromosome 17, and female gametes with deficiency. It is possible, however, that not all types were equally capable of fertilization. In particular, in view of the known effects of t -alleles on male segregation ratio, it may be that the male gametes which were respectively Tt^{h2} and nullo- t differed in fertilizing capacity. Although the allele t^{h2} is not known to affect segregation ratio in chromosomally normal (non- $T138$) animals¹³ perhaps it might do so in other cases. Moreover, Dunn and Bennett^{14,15} described a mutation *Low* at another locus in this region of chromosome 17, which also affected male segregation ratio. Hence, duplication or deficiency of this locus could also affect the observed segregation of non-disjunctional offspring.

Another possible explanation is that the frequencies of formation of the relevant gametes were different in the two types of cross, through different rates of occurrence of adjacent-2 disjunction during meiosis. There was a clear difference between the males of the reciprocal crosses in

frequency of quadrivalent formation at meiosis¹⁶, but further work is needed to establish whether this was the cause of the observed difference in frequency of $Tt^{h2} cwcw$ offspring.

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¹⁴C-Catecholamine Synthesis in Mouse Brain during Morphine Withdrawal

AFTER a single injection of morphine or related narcotic analgesics, incorporation of ¹⁴C-tyrosine into ¹⁴C-catecholamines is increased markedly in the brains of mice^{1,2} and rats³. However, repeated administration of these drugs results in the development of tolerance to their effects upon ¹⁴C-catecholamine synthesis^{1,2}. We have determined that once complete tolerance has developed, the mouse brain cannot maintain normal rates of catecholamine synthesis without the continued administration of morphine.

Brain contents of ¹⁴C-dopamine and ¹⁴C-noradrenaline were determined 40 min after the injection of ¹⁴C-tyrosine (55 µg kg⁻¹; specific activity, 410 mCi/mmol, uniformly labelled, New England Nuclear Corporation) into the tail vein of the female albino mouse (20–30 g). Maximum incorporation of ¹⁴C-tyrosine into ¹⁴C-catecholamines in the brain occurred 40 min after injection of labelled tyrosine¹. Thirty minutes prior to the administration of ¹⁴C-tyrosine, either morphine sulphate, 30 mg kg⁻¹, or saline was injected intraperitoneally. The maximum incorporation with this schedule of injections also occurred 40 min after the administration of ¹⁴C-tyrosine. Therefore, the incorporation of ¹⁴C-tyrosine into ¹⁴C-catecholamine was always determined 70 min after morphine administration and 40 min after injection of ¹⁴C-tyrosine. Labelled noradrenaline and dopamine were separated on 'Dowex 50' Na⁺ columns (X8, 200–400 mesh) as previously described⁴.

To produce tolerance, we gave 1–12 morphine sulphate injections, 100 mg kg⁻¹, intraperitoneally at 6 h intervals. Six hours after the last injection, either saline or morphine sulphate, 30 mg kg⁻¹, was administered, followed 30 min later by an injection of ¹⁴C-tyrosine. Incorporation of ¹⁴C-tyrosine into ¹⁴C-catecholamines was not changed significantly in the brains of mice receiving saline after pretreatment with varying numbers of morphine injections (Fig. 1). Morphine, 30 mg kg⁻¹, induced greater incorporation of ¹⁴C-tyrosine into ¹⁴C-dopamine and ¹⁴C-noradrenaline in the brains of mice receiving

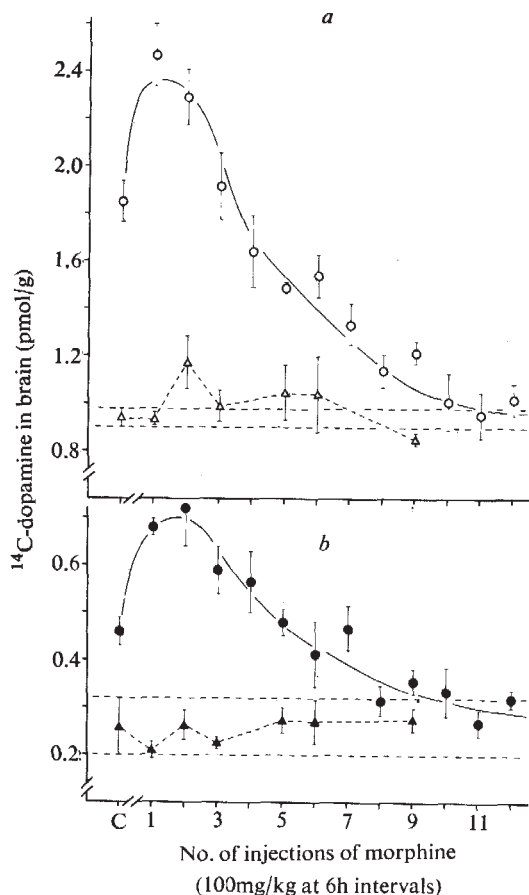


Fig. 1 Development of tolerance to morphine-induced increases in incorporation of ^{14}C -tyrosine into ^{14}C -dopamine (a) and ^{14}C -noradrenaline (b) in mouse brain. Mice were given varying numbers of injections of morphine (100 mg kg^{-1} at 6 h intervals). Effects of either morphine (30 mg kg^{-1}) (●, ○) or saline (▲, △) upon incorporation of ^{14}C -tyrosine were determined 6 h after the last injection of morphine (100 mg kg^{-1}). C, Determinations on non-tolerant mice injected with saline or a single dose of morphine (30 mg kg^{-1}). Each point represents the mean of at least 6 determinations. Vertical bars and horizontal broken lines represent standard errors.

morphine for the first time ($P < 0.005$, Fig. 1). Morphine, 30 mg kg^{-1} , produced a smaller response in mice previously treated with three or more injections of morphine, 100 mg kg^{-1} . The ability of the mouse brain to respond to morphine decreased as the number of injections of morphine, 100 mg kg^{-1} , increased, demonstrating the development of tolerance to the effect of morphine upon incorporation. After eight injections, morphine, 30 mg kg^{-1} , caused no significant increase in incorporation of ^{14}C -tyrosine into ^{14}C -catecholamines in the brain, indicating the development of complete tolerance.

One explanation is that morphine has lost its ability to increase the incorporation of ^{14}C -tyrosine into ^{14}C -catecholamines in the mouse brain. Morphine might also now be necessary for the brain to synthesize noradrenaline and dopamine at normal rates. To test this, we administered morphine, 100 mg kg^{-1} , to mice every 6 h for a total of 9 injections. After the ninth injection, the mice were withdrawn from morphine for periods ranging from 6 to 72 h. At various periods of time after the onset of morphine withdrawal, either saline or morphine sulphate, 30 mg kg^{-1} , was administered, followed 30 min later by an injection of ^{14}C -tyrosine. From eighteen to fifty-four hour after the onset of withdrawal, the mouse brain incorporated significantly less ^{14}C -tyrosine into both labelled catecholamines (Fig. 2). The largest decrease in synthesis occurred 36 h after the last morphine injection ($P < 0.005$). Subsequently, the mouse brain gradually recovered its ability to make ^{14}C -catecholamines.

During the withdrawal period, as the brain regained its ability to synthesize catecholamines, it once more became responsive to the effects of morphine upon incorporation of ^{14}C -tyrosine and ^{14}C -dopamine and ^{14}C -noradrenaline (Fig. 2). Morphine, 30 mg kg^{-1} , administered after 66 h of withdrawal, had the same effect on incorporation in previously tolerant mice as it did in naive mice never made tolerant to morphine. At all times during the first 66 h of withdrawal, morphine, 30 mg kg^{-1} , restored the incorporation of ^{14}C -tyrosine in the mouse brain to a level higher than or equal to that seen in mice never treated with morphine. This indicates that continued morphine administration is necessary for fully tolerant mice to incorporate normal amounts of labelled tyrosine into labelled noradrenaline and dopamine in the brain.

The decrease in synthesis of ^{14}C -catecholamines observed during withdrawal could be due to a decrease in the specific activity of the pool of labelled tyrosine in the brain or to an increased catabolism of catecholamines rather than to a decrease in the rate of synthesis of ^{14}C -noradrenaline and ^{14}C -dopamine. To evaluate these possibilities, we determined the specific activities of ^{14}C -tyrosine, ^{14}C -dopamine, and ^{14}C -noradrenaline after the abrupt withdrawal of morphine. At various times after the onset of withdrawal, the levels in the brain of endogenous and labelled tyrosine, dopamine, and noradrenaline were determined^{2,4,5} and their specific activities calculated (Table 1).

Withdrawal from morphine had no effect on the endogenous noradrenaline, dopamine, free tyrosine or ^{14}C -tyrosine content

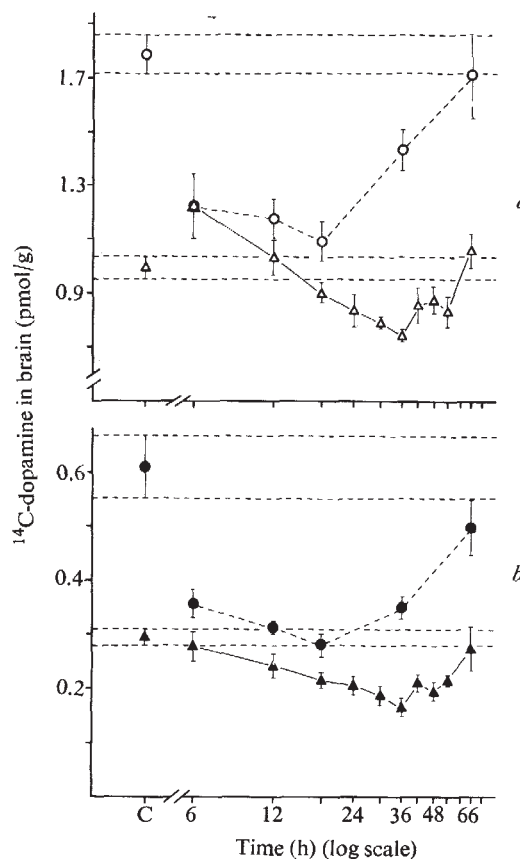


Fig. 2 Decreased incorporation of ^{14}C -tyrosine into ^{14}C -dopamine (a) and ^{14}C -noradrenaline (b) in the brains of morphine-tolerant mice during withdrawal. Mice were made tolerant with 9 injections of morphine (100 mg kg^{-1} at 6 h intervals). Effects of either saline (▲, △) or morphine (30 mg kg^{-1}) (●, ○) were determined at varying intervals of time after onset of the morphine-withdrawal period. C, Determinations on non-tolerant mice injected with saline or a single dose of morphine (30 mg kg^{-1}). Each point represents the mean of at least 6 determinations. Vertical bars and horizontal broken line represent standard errors.

Table 1 Specific Activities of ^{14}C -Noradrenaline, ^{14}C -Dopamine, and ^{14}C -Tyrosine in the Brains of Morphine-tolerant Mice at Varying Intervals of Time after the Onset of the Morphine-withdrawal Period

Time after onset of withdrawal (h)	^{14}C -Noradrenaline ($\mu\text{mol mol}^{-1}$)	^{14}C -Dopamine ($\mu\text{mol mol}^{-1}$)	^{14}C -Tyrosine ($\mu\text{mol mol}^{-1}$)
C	110.7 $\pm$ 7.3	171.4 $\pm$ 7.2	45.5 $\pm$ 8.4
6	91.4 $\pm$ 8.9	151.5 $\pm$ 4.9	50.6 $\pm$ 4.7
18	*79.6 $\pm$ 5.4	*131.7 $\pm$ 6.3	38.0 $\pm$ 2.0
36	*66.8 $\pm$ 6.9	*122.2 $\pm$ 2.8	40.8 $\pm$ 4.1
54	*86.9 $\pm$ 4.1	*116.7 $\pm$ 7.8	46.9 $\pm$ 4.6
72	142.8 $\pm$ 18.3	*127.9 $\pm$ 13.9	43.5 $\pm$ 6.8

Specific activities refer to the brain content of ^{14}C -noradrenaline, ^{14}C -dopamine and ^{14}C -tyrosine in $\mu\text{mol g}^{-1}$ of tissue wet weight expressed as a fraction of the total brain content of noradrenaline, dopamine or free tyrosine in mol g^{-1} of tissue. Mice were made tolerant with 9 injections of morphine (100 mg kg^{-1} at 6 h intervals). Specific activities were determined at varying intervals of time after onset of morphine-withdrawal period. C=Determinations on non-tolerant mice injected with saline. Each specific activity represents the mean of at least five determinations.

* Indicates values which are significantly different from control. ($P < 0.05$.)

of the brain at 40 min after the intravenous injection of labelled tyrosine. During withdrawal, the specific activity of ^{14}C -noradrenaline and ^{14}C -dopamine in the brain decreased. The most significant decrease in the specific activities of both amines occurred 36 h after the onset of withdrawal ($P < 0.005$), indicating that their rate of synthesis decreases during withdrawal.

Our study suggests that catecholamines play an important role in the mechanisms by which morphine-like drugs produce physical dependence. The action of morphine's on catecholamine synthesis in the brain of the mouse is a specific biochemical effect of the narcotic analgesics^{1,2}. Naloxone, a narcotic blocking agent, antagonizes morphine-induced increases in the incorporation of ^{14}C -tyrosine into ^{14}C -noradrenaline and ^{14}C -dopamine in the mouse brain². As with all other specific effects of the narcotic analgesics, tolerance and cross-tolerance develop to the effects of morphine upon brain catecholamine synthesis^{1,2}. The schedule of morphine injections necessary to produce maximum tolerance in the present study was previously found to produce tolerance to a variety of other specific effects of the narcotic analgesics⁶. Continued morphine administration in this study not only produces tolerance to the specific effects of this drug but produces physical dependence as well. In this study, the mouse brain, after nine injections of morphine, could not synthesize normal amounts of labelled catecholamines from labelled tyrosine without the continued administration of morphine. Thus, optimal synthesis and turnover of ^{14}C -catecholamines in the brain of the morphine-tolerant mouse is dependent upon the continued administration of morphine.

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Relationship between Serum and Cerebrospinal Fluid Folate

ALTHOUGH a relationship between vitamin B_{12} deficiency and neuropsychiatric illness is well established, the effects of folic acid deficiency on the nervous system are less certain. It has been noted that the administration of folic acid to patients with pernicious anaemia could aggravate or precipitate nervous system complications¹, and it has been widely assumed that deficiency of folic acid does not produce nervous system dysfunction. This assumption has been questioned recently on the basis of studies in epileptic and psychiatric patients²⁻⁵. The need for a re-evaluation of the relationship of folate deficiency to nervous system disorders is underlined by the relatively high concentrations of folate in the cerebrospinal fluid (CSF)⁶. We have therefore examined the relationship between serum and CSF folate concentrations in a group of neurological controls, psychiatric patients and drug treated epileptic patients.

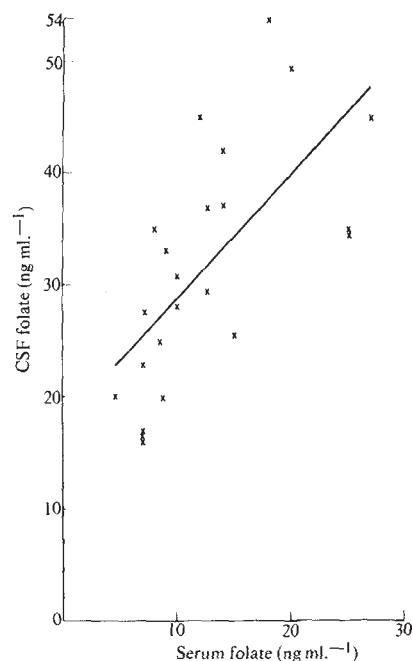


Fig. 1 Relationship of serum and CSF folate in controls.

Serum and CSF folate were assayed by the aseptic technique of Herbert⁷ in three groups of patients. (1) Twenty-three controls, mean age 44 yr, range 29-68; undergoing myelography for back or root pain. (2) Fourteen psychiatric patients, mean age 39.3 yr, range 17-58, all of whom were acute admissions to the Connecticut Mental Health Center with a wide range of diagnoses. Serum and CSF folate were assayed before the commencement of psychotropic drug therapy. (3) Forty-six epileptic patients, mean age 39 yr, range 14-63, from the seizure clinics of the Yale New Haven and West Haven VA Hospitals. All were treated with various combinations of diphenylhydantoin, phenobarbitone and primidone and, in some cases, other anticonvulsant or psychotropic drugs. The mean duration of anticonvulsant therapy was 15 yr, range 1-43 yr.

Venepuncture was always undertaken at the same time as lumbar puncture. In groups 2 and 3 this was at 8 a.m., in the fasting state. In group 1 the myelograms were carried out at variable times of the day. As folate was found to be log normally distributed in both serum and CSF, significance of differences between means and correlation coefficients has been calculated from logarithmically transformed data.

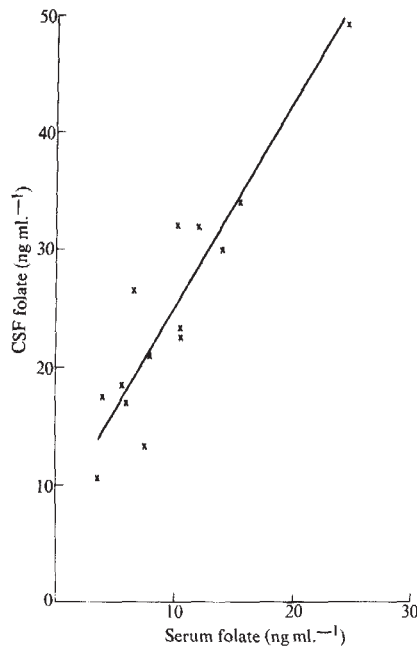


Fig. 2 Relationship of serum and CSF folate in psychiatric patients.

There was a significant fall in folate concentrations in both serum and CSF in the epileptic patients when compared with controls ($P < 0.001$) or with psychiatric patients ($P < 0.05$) (Table 1). Folate concentrations in the psychiatric patients were intermediate between control and epileptics but the difference from controls was not quite statistically significant. In all three groups there was a high degree of correlation between serum and CSF folate (Figs. 1–3). The increasing steepness of the slope of the regression lines in Figs. 1–3 shows that with increasing folate deficiency the relationship between serum folate and CSF folate is changing. This is confirmed by the observation that the best fit for the combined data in Fig. 4 is a curve. Initially the serum folate appears to fall more rapidly than CSF folate, following which the rate of fall of CSF folate increases. There is no evidence that anticonvulsant drugs alter the relationship between serum and CSF folate directly, as there is no significant difference between the slopes of the regression lines for controls and for epileptic patients with folate concentrations within the control range. This agrees with observations on the relationship between serum and red cell folate concentrations in drug treated epileptic patients⁸.

It is well known that anticonvulsant therapy will result in a fall in serum folate concentrations in a high proportion of epileptic patients^{1,9}. This study confirms earlier reports^{10,11} of an associated fall in CSF folate in such patients although this was not observed by others^{12,13}.

Our findings indicate that changes in serum folate concentrations are accompanied by corresponding changes in the nervous

system. But it should be noted that during treatment with folic acid there is a striking alteration in the relationship between serum and CSF folate, for although serum folate

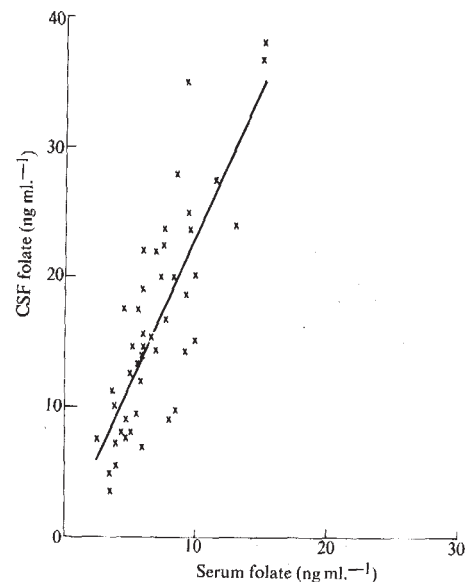


Fig. 3 Relationship of serum and CSF folate in drug treated epileptic patients.

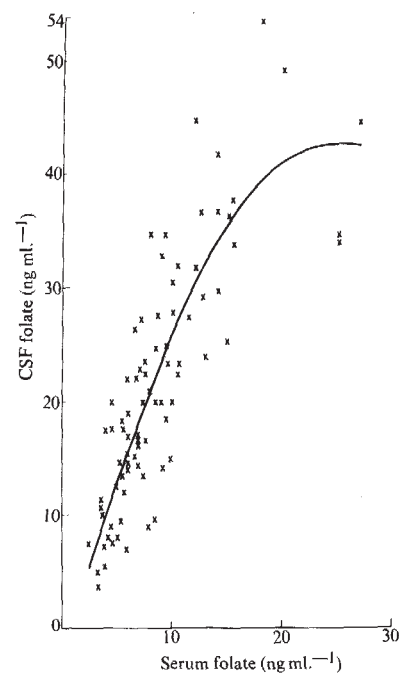


Fig. 4 Relationship of serum and CSF folate in combined groups.

Table 1 Serum and CSF Folate Concentrations, Regression Equations and Correlation Coefficients

	Number	Mean serum folate (μg/ml.)	Mean CSF folate (μg/ml.)	Regression equation* and significance of the regression coefficient	Correlation coefficient and significance
Controls	23	12.54	31.63	$y = 1.11x + 17.75$ ($P < 0.001$)	0.73 ($P < 0.001$)
Psychiatric patients	14	9.90	24.91	$y = 1.74x + 7.69$ ($P < 0.001$)	0.87 ($P < 0.001$)
Epileptic patients	46	7.02†	16.15†	$y = 2.29x + 0.29$ ($P < 0.001$)	0.79 ($P < 0.001$)
Combined data	83	9.04	21.92	$y = -4.75 + 3.91x - 0.08x^2$	0.79 ($P < 0.001$)

* y , serum folate; x , CSF folate.

† Significance of differences from mean of controls, $P < 0.001$; and from mean of psychiatric patients, $P < 0.05$.

concentrations rapidly rise to very high levels, CSF folate concentrations either rise very slowly¹⁴ or not at all¹⁵.

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Nature of the Molecular Defect in Phenylketonuria and Hyperphenylalaninaemia

Two forms of phenylketonuria (PKU) have been described at the biochemical level: (1) classical PKU in which no hepatic phenylalanine hydroxylase activity has been found¹⁻⁴, and (2) a typical PKU or hyperphenylalaninaemia in which about 5% of the normal hydroxylase activity is present⁵. * Whereas it seems most probable that classical PKU results from a structural gene mutation, the hyperphenylalaninaemic syndrome could result from either a structural or a regulatory gene mutation.

Recently we were able to study a liver biopsy sample from an atypical PKU patient and two from classical PKU patients. With an assay in which all the known components were added in excess⁷ and which could have detected 1% of the normal hydroxylase activity, we have found, in confirmation of our previous results^{4,5}, that the atypical PKU liver had 5-7% of the normal hydroxylase activity; the classical PKU samples had no detectable hydroxylase activity.

* Using an enzyme assay in which all of the essential components of the hydroxylating system were not added (but may have been present in the liver extract), Justice *et al.*⁶ found activities of 10% and 43% of normal for two hyperphenylalaninaemic patients.

Results of a study of some of the immunological and kinetic properties of the hydroxylase in the hyperphenylalaninaemic liver strongly suggest that the enzyme in this patient is structurally distinct from the hydroxylase present in normal human liver. In the classical PKU liver samples, which were devoid of hydroxylase activity, no cross-reacting protein could be detected.

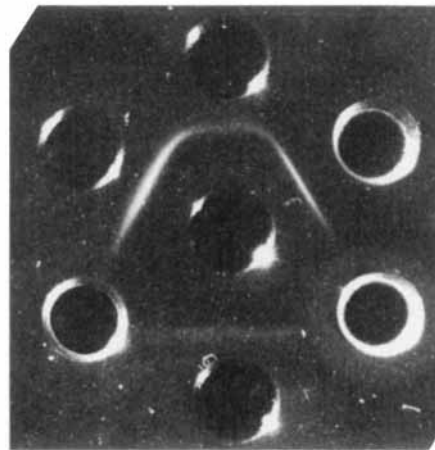


Fig. 1 Double immunodiffusion reaction. The centre well contained antiserum to rat liver phenylalanine hydroxylase. Peripheral wells were filled as follows: 12 o'clock, purified rat liver phenylalanine hydroxylase (100 µg/ml.); 2 o'clock, 0-50% ammonium sulphate fraction of normal liver extract (65 mg/ml.); 4 o'clock, 0-50% ammonium sulphate fraction of atypical PKU liver extract (62 mg/ml.); 6 o'clock, purified rat liver phenylalanine hydroxylase; 8 o'clock, atypical PKU liver extract (31 mg/ml.); 10 o'clock, rat liver extract (32 mg/ml.). Extracts were obtained from homogenates of liver tissue (1:3 w/v with 0.15 M KCl) by centrifuging at 30,000g for 45 min. Extracts were brought to 50% of saturation with a saturated solution of ammonium sulphate; the pellet obtained from centrifugation was dissolved in one-tenth the original volume of the extract with 0.01 M Tris-HCl, pH 7.0, containing 0.12 M KCl. Each well contained 0.007 ml. Incubation was at 4° C; the photograph was taken after 18 h.

A specific antiserum to rat liver phenylalanine hydroxylase, which cross-reacts with the enzyme from the human liver, was produced in sheep⁸. Fig. 1 shows that in double immunodiffusion reactions the antiserum forms a single precipitin line with rat liver phenylalanine hydroxylase. While a precipitin line of identity forms with the ammonium sulphate fraction from the normal human liver, no line forms with either the extract or the ammonium sulphate fraction from the hyperphenylalaninaemic liver. Serial dilutions of the ammonium sulphate fraction of the normal liver reveal a precipitin line at as low as a 1:10 dilution. Serial dilutions of the hyperphenylalaninaemic extract, as well as the extract concentrated by ammonium sulphate precipitation (0-50% saturated) and of the protein that remained soluble at 50% ammonium sulphate saturation, fail to form precipitin lines in double diffusion reactions. Cross-reactivity of the antiserum with the atypical PKU extract was demonstrable, however, if the extract (0.7 mg protein) was preincubated with antiserum. After 3 h at 2° C no precipitate formed, but the activity of the enzyme was inhibited: 0.5 µl. antiserum, 45% inhibition; 0.8 µl. antiserum, 51% inhibition; 2 µl. antiserum, 53% inhibition. (Control serum was used to make up residual serum volume in all tubes.)

These data eliminate the possibility that a mutant, but antigenically-identical, phenylalanine hydroxylase is present in atypical PKU liver at greater than 10% of the concentration present in normal liver. Such a mutation has been described recently for galactosaemia⁹. Our data are compatible with the existence of either (1) a regulatory mutation leading to a steady state concentration of normal phenylalanine hydroxylase

of less than 10% of that present in normal liver, or (2) a structural gene mutation resulting in an enzyme of unknown concentration that retains at least some antigenic determinants in common with the normal enzyme.

We have attempted to distinguish between these two possibilities. Extracts from the normal and hyperphenylalaninaemic livers were compared with respect to their apparent K_m values for the synthetic cofactor, 6,7-dimethyltetrahydropterin (DMPH_4), and for L-phenylalanine. Whereas the apparent K_m value for DMPH_4 is 0.005 mM for both, the apparent K_m values for L-phenylalanine for the normal liver and for the hyperphenylalaninaemic liver are 1.25 mM and 0.62 mM, respectively (Fig. 2). In two previous studies^{5,10}, the apparent K_m s for phenylalanine with normal liver were 1.20 mM and 1.25 mM whereas the values for two different hyperphenylalaninaemic livers were 0.67 mM and 0.88 mM, respectively. In the present study we have used a more detailed L-phenylalanine concentration curve, and it seems highly unlikely that the difference observed derives from experimental variation.*

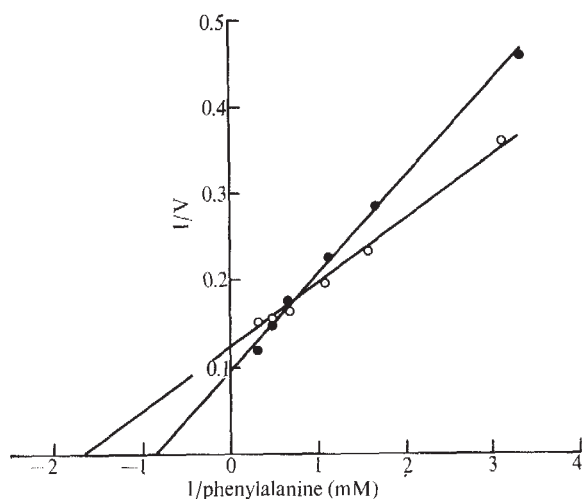


Fig. 2 The effect of L-phenylalanine concentration on the rate of tyrosine formation catalysed by normal liver and atypical PKU liver phenylalanine hydroxylases. Phenylalanine hydroxylase activity was determined from the conversion of ^{14}C -L-phenylalanine to tyrosine as has been described⁷. Assay volume was 0.2 ml.; incubation was for 60 min at 25° C. L-Phenylalanine concentrations have been corrected for endogenous phenylalanine levels. ●, 0.02 ml. (0.12 mg protein) per assay of normal liver extract (from a 1:11 w/v homogenate with 0.15 M KCl); ○, 0.05 ml. (0.70 mg protein) per assay of atypical PKU liver extract (from a 1:5 w/v homogenate with 0.15 M KCl). Velocity is measured in nmol tyrosine formed in 60 min.

A second property that is different for the two hydroxylases is the degree of their stimulation by lysolecithin. Rat liver phenylalanine hydroxylase¹¹, and to a lesser extent human liver phenylalanine hydroxylase (unpublished observations of P. A. F. and S. K.), are stimulated by lysolecithin with tetrahydrobiopterin as cofactor. Fig. 3 shows that the hydroxylase activity in the normal liver extract can be stimulated about five-fold with increasing lysolecithin concentration, whereas activity in the extract from the hyperphenylalaninaemic liver is stimulated less than two-fold. The following observations make highly unlikely the premise that differences in endogenous phospholipids (or other substances) in the two extracts account for the differential effect with lysolecithin.

* Clinically and pathologically the patient from whom the present hyperphenylalaninaemic liver biopsy was obtained had evidence of subclinical hepatitis. Since the liver had the expected level of hydroxylase activity and since the kinetic properties observed here are virtually the same as those found with the previous hyperphenylalaninaemic livers, it seems only remotely possible that the viral infection affected either the level or character of the phenylalanine hydroxylase in this liver.

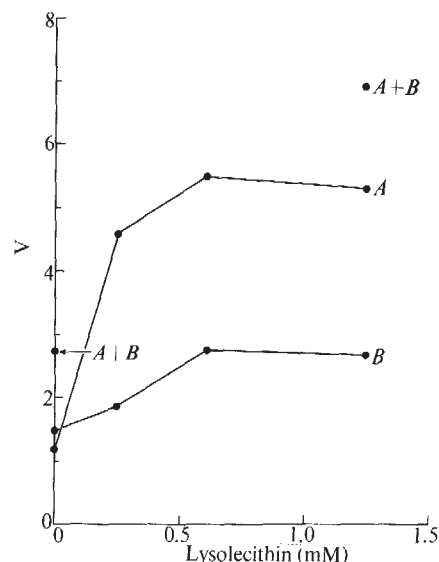


Fig. 3 The effect of lysolecithin on the rate of tyrosine formation catalysed by normal liver and atypical PKU liver phenylalanine hydroxylases. Assay was as described in Fig. 2 with the following exceptions: phenylalanine concentration was 0.1 mM; tetrahydrobiopterin (0.014 mM) replaced DMPH_4 as cofactor; lysolecithin was present in each assay at the concentration indicated. A, 0.02 ml. normal liver extract; B, 0.05 ml. atypical PKU liver extract.

(1) Total lipid phosphorus levels in the two extracts show their contribution to be only 2.5–5% of that contributed by lysolecithin at the highest two lysolecithin levels. (2) Mixing the two extracts without added lysolecithin results in hydroxylase activity that is additive compared with the activities of each extract alone; mixing the two extracts is nearly additive in the presence of lysolecithin (Fig. 2); thus, there are neither soluble activators in the atypical PKU extract that stimulate normal hydroxylase nor soluble inhibitors that interfere significantly with the response of the normal enzyme to lysolecithin. (3) Lysolecithin stimulation of normal human liver extract is the same as that seen with purified normal human liver phenylalanine hydroxylase (unpublished observations of P. A. F. and S. K.).

The rate of heat inactivation of the hydroxylase activity in the two extracts also differs. After 2 and 4 min at 50° C, the normal enzyme lost 27% and 59% of its activity, respectively. In the same conditions, the enzyme from the hyperphenylalaninaemic liver lost 58% and 68% of control activity, respectively.

Two classical PKU liver samples were also studied. Fig. 4 shows a double immunodiffusion reaction with classical PKU liver. Here, too, no cross-reacting material could be detected. The spurs on the rat phenylalanine hydroxylase precipitin lines at their intersection with the normal human liver phenylalanine hydroxylase line appear with prolonged incubation of the plates (similar spurs were seen in the plate in Fig. 1 with doubling of the incubation time). Thus, as we have reported⁸, normal human phenylalanine hydroxylase shares antigenic sites with the rat enzyme but is not antigenically identical to it.

Our observations are consistent with the interpretation that the phenylalanine hydroxylase in the atypical PKU liver studied here (and, most likely, in the earlier two studies^{5,10}) is a structurally altered enzyme compared with the hydroxylase from normal liver. Among other less likely possibilities, the most parsimonious explanation for the alteration is that the enzyme is a product of a structural gene mutation. Although persistence of a foetal isozyme might account for our observations, Barranger *et al.*¹² concluded that the foetal enzyme of rat liver has an apparent K_m for phenylalanine not significantly different from those of the isozymes that are predominant in

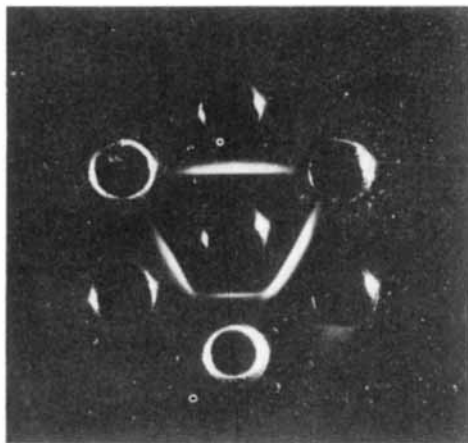


Fig. 4 Double immunodiffusion reaction. Conditions and preparation of samples are as described in Fig. 1. The centre well contained antiserum. Peripheral wells were filled as follows: 12 o'clock, purified rat liver phenylalanine hydroxylase (350 μ g/ml.); 2 o'clock, classical PKU liver extract (19 mg/ml.); 4 o'clock, purified rat liver phenylalanine hydroxylase; 6 o'clock, 0-50% ammonium sulphate fraction of normal liver extract (40 mg/ml.); 8 o'clock, rat liver extract (32 mg/ml.); 10 o'clock, 0-50% ammonium sulphate fraction of classical PKU liver extract (31 mg/ml.). The photograph was taken after 30 h incubation at 4° C.

adult rat liver. The limited number of samples that have been studied, as well as the multiplicity of molecular events that could lead to a similar phenotypic expression, preclude a firm statement that all hyperphenylalaninaemic individuals possess the same molecular defect.

We cannot say a great deal about classical PKU except that again, unlike the well documented case of galactosaemia⁹, 10% or more of an antigenically identical cross-reacting protein is not present. It should be emphasized, however, that our results demonstrate directly for the first time what has been suggested from activity measurements; phenylalanine hydroxylase is deficient in classical PKU. Since the presence of an altered enzyme molecule, as opposed to its absence (deletion mutation), might have therapeutic implications, we are currently engaged in the development of a radioimmunoassay in an attempt to look for lower levels of cross-reacting protein in classical PKU.

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Prevention of Pairing of Homoeologous Meiotic Chromosomes of Wheat by an Activity of Supernumerary Chromosomes of *Aegilops*

THE restriction of meiotic pairing to homoeologous chromosomes in *Triticum aestivum* ($2n=6x=42$) is under the control of a locus (*Ph*) on the long arm of chromosome 5B^{1,2}. Two 14-chromosome diploid relatives of wheat, *Aegilops speltoides* and *Aegilops mutica*, have genotypes that can suppress the activity of *Ph*. Hybrids between wheat and these *Aegilops* spp. show extensive pairing of homoeologous chromosomes of the *A*, *B* and *D* genomes. Hybrids between wheat and other species in the genus *Aegilops* show no suppression of *Ph* activity. On this evidence it has been suggested that the *Ph* allele is recessive to a dominant condition found in *Ae. speltoides* and *Ae. mutica* and that possibly the allele in wheat originated by mutation during or soon after the combination of the *A* and *B* genomes in tetraploid wheat.

It has, however, recently been shown that wheat/*Ae. mutica* hybrids segregate into four classes with different levels of meiotic chromosome pairing³. The segregation was consistent with the presence of two loci each with two alleles in *Ae. mutica* that determine the extent of homoeologous pairing. There were classes of wheat/*Ae. mutica* hybrids with means of 1.51, 4.13, 7.06 and 12.91 chiasmata per cell. The lower class indicates the presence of alleles in *Ae. mutica* which do not suppress the effect of the *Ph* allele of wheat, or which themselves actively inhibit homoeologous pairing.

Similar analysis of pairing in *F*₁ hybrids of *T. aestivum* × *Ae. speltoides*, with and without supernumerary chromosomes, has revealed the occurrence of allelic variation in populations of *Ae. speltoides* affecting homoeologous meiotic pairing⁴.

If the activity performed by chromosome 5B of *T. aestivum* was carried out when this chromosome was first incorporated in polyploid wheat a similar activity might still be found in contemporary diploids derived from the ancestor of wheat that contributed the *B* genome. It may be that those genotypes of *Ae. speltoides* and *Ae. mutica* that do not cause homoeologous pairing, in hybrids with wheat, represent diploids with activities like that of 5B. If this were so, in wheat/*Aegilops* hybrids lacking chromosome 5B, compensation should occur for the absence of 5B, resulting in the continued inhibition of homoeologous pairing.

We have tested this by constructing hybrids from the crosses, *T. aestivum* monosomic 5B ($2n=41$) × *Ae. mutica* ($2n=14$) and *T. aestivum* nullisomic 5B tetrasomic 5D ($2n=42$) × *Ae. mutica* ($2n=14$). The *Ae. mutica* parents were drawn from a population containing plants heterozygous at the loci influencing the level of homoeologous pairing. The monosomic 5B wheat parent gave rise to 28- and 27-chromosome hybrids in which chromosome 5B was respectively present or absent. In the 28-chromosome hybrids derived from the nullisomic 5B tetrasomic 5D parent, chromosome 5B was always absent and chromosome 5D was disomic. All the hybrids were grown in controlled environment cabinets at 20° C with continuous light and chiasma frequency was scored usually in 50 cells per plant.

Segregation for various levels of homoeologous pairing occurred in hybrids carrying chromosome 5B (Table 1) indicating the heterozygosity of its *Ae. mutica* parents at the loci capable of suppressing the *Ph* effect (Fig. 2b). However, 27-chromosome hybrids, deficient for chromosome 5B and derived from the same parents, all had high levels of homoeologous pairing, as did all of the hybrids derived from the nullisomic 5B tetrasomic 5D wheat parent. There was, therefore, no evidence that in genotypes corresponding to those in which the *Ph* activity was not inhibited, the contribution of *Ae. mutica* was able to compensate for the absence of

chromosome 5B. This demonstrates that the regulation of meiotic chromosome pairing in polyploid wheat, as a result of which synapsis is confined to full homologues, could not have arisen through the incorporation of a genetic condition like that found in *Ae. mutica* lacking the capacity to suppress the *Ph* effect. This suggests that similar variation in *Ae. speltoides* is unlikely to have been the source of the present genetic condition of wheat.

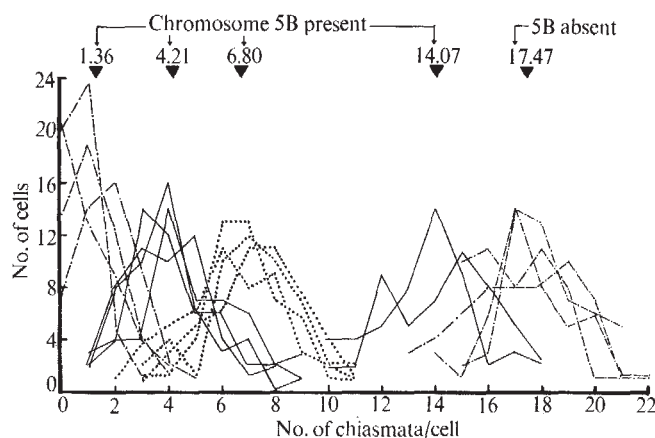


Fig. 1 Between family frequency distribution curves for number of chiasmata/cell in hybrids of *Triticum aestivum* × *Aegilops mutica* with and without wheat chromosome 5B. Curves, drawn from plants having fifty scored cells, fall into five categories; the means of the categories are as indicated.

The overall mean of 16.82 chiasmata per cell in hybrids lacking 5B was somewhat higher than that usually encountered in the category of cells with the highest pattern of pairing in plants carrying 5B. Fig. 1 shows that this "super high" pairing category which was always occupied by 5B-deficient hybrids is distinct from those occupied by hybrids carrying 5B. Moreover, super high pairing occurred irrespective of the genetic contribution of *Ae. mutica*. This implies that a 5B activity imposed some restraint on the level of homoeologous pairing even when the effect of *Ph* was apparently inhibited by the *Ae. mutica* component of hybrids. This may result from the incomplete inactivation of *Ph* or from the continuation of some other activity of chromosome 5B.

Some individuals of *Ae. mutica* carry supernumerary (or B) chromosomes⁵. Similar segregation into four categories with different levels of homoeologous pairing occurred in *T. aestivum* × *Ae. mutica* hybrids to which supernumeraries had been transmitted by the *Ae. mutica*⁴. Thus, in the presence of wheat chromosome 5B, the *Aegilops* supernumeraries apparently had no effect on the pattern of meiotic chromosome pairing (Table 2). There was similarly no effect of supernumeraries transmitted to *T. aestivum* × *Ae. speltoides* hybrids by the *Aegilops* parent⁴.

Table 1 Mean Chiasma Frequencies of F₁ Hybrids with and without Chromosome 5B

Chromosome 5B	Pairing class	No. hybrids	Mean chiasma/cell Expected*	Observed	Range chiasma/cell
Present	Low	—	1.51	—	—
	Intermediate (low)	5	4.13	4.48 ± 0.23	3.25–5.88
	Intermediate (high)	—	7.06	—	—
	High	7	12.91	12.09 ± 0.11	11.39–13.00
Absent	Super high	101	—	16.82 ± 0.01	14.20–18.80

Derived from the crosses *T. aestivum* mono-5B × *Ae. mutica* and *T. aestivum* nulli-5B tetra-5D × *Ae. mutica*.

* On the basis of previous observations of Dover and Riley³.

Table 2 Mean Chiasma Frequencies of F₁ Hybrids with Supernumerary Chromosomes and with or without Chromosome 5B

Pairing class	Chromosome 5B	
	Present *	Absent *
Low	2.09 (1–4)	—
Intermediate (low)	4.47 (2–3)	3.67 (2)
Intermediate (high)	7.44 (2–3)	—
High	13.22 (1–3)	—

Derived from the crosses *T. aestivum* euploid or mono-5B × *Ae. mutica* with supernumeraries (number of supernumeraries in parentheses).

* Overall mean of class taken from Vardi and Dover⁴.

Recently, however, chiasma frequencies have been scored in hybrids obtained from crosses, *T. aestivum* monosomic 5B × *Ae. mutica* with supernumerary chromosomes and *T. aestivum* monosomic 5B × *Ae. speltoides* with supernumerary chromosomes. The supernumerary chromosomes are smaller than the remainder of the complement and are readily recognizable in preparations made from mitotic and meiotic cells. Only hybrids carrying supernumeraries from these crosses were scored for chiasma frequencies, after having been grown in controlled environment chambers at 20° C with continuous light.

We have already established⁴ that hybrids from both crosses, in which chromosome 5B was present, segregated into the four pairing categories originally described for *T. aestivum* × *Ae. mutica* hybrids by Dover and Riley³. Hybrids to which chromosome 5B had not been transmitted, however, all had a low level of meiotic pairing (Tables 2 and 3). Thus, the presence



Fig. 2 a, Pollen mother cell of *Triticum aestivum* nullisomic 5B tetrasomic 5D × *Aegilops mutica* (2n=28; 5B absent) (super high pairing class) 4 univalents, 5 bivalents, 2 trivalents and 2 quadrivalents. b, Pollen mother cell of 28-chromosome hybrid (5B present) derived from cross of *Triticum aestivum* monosomic 5B × *Aegilops mutica* (low-pairing class) 24 univalents, 2 bivalents.

of supernumerary chromosomes in *5B* deficient hybrids resulted in a marked reduction in the extent of homoeologous pairing in pronounced contrast to the super high pairing that always occurred in the absence of *5B*.

Table 3 Mean Chiasma Frequencies of F_1 Hybrids, with Supernumerary Chromosomes and with or without Chromosome *5B*

Pairing class	Chromosome <i>5B</i>	
	Present *	Absent *
Low	0.93 (2)	0.98 (2)
Intermediate (low)	3.27 (1-4)	2.65 (2)
Intermediate (high)	9.32 (1-6)	—
High	16.30 (1-5)	19.93 (0)

Derived from the crosses *T. aestivum* euploid or mono-*5B* × *Ae. speltoides* with supernumeraries (number of supernumeraries in parentheses).

* Overall mean of class taken from Vardi and Dover⁴.

Indeed the presence of supernumerary chromosomes created a situation in which there was compensation for the absence of chromosome *5B* of wheat. Similar effects of supernumerary chromosomes on homoeologous meiotic pairing have been reported in *Lolium*⁶.

When *5B* was absent there was no clear segregation into different pairing categories either in the presence or absence of supernumeraries. Thus, segregation of different allelic conditions at the two pairing-control loci of *Ae. mutica* or *Ae. speltoides* is only revealed phenotypically when *5B* is present.

Previous consideration of the origin of the control of the diploid-like meiotic chromosome pairing of polyploid wheat, by chromosome *5B*, had led to the conclusion that the present activity of the *Ph* locus may have arisen as a result of mutation at the time of, or soon after, the origin of the polyploid⁷. This conclusion was reached because of the failure to detect, among any of the diploid relatives of wheat, a genetic effect resembling that performed by chromosome *5B*. All the diploid genotypes either failed to compensate for the absence of *5B* by preventing homoeologous pairing, or they suppressed the activity by which homoeologous pairing was normally prevented. Previously these alternative effects were thought to characterize species, but the present and other results^{3,4,8} have shown that the same genetic distinctions can occur within species. Our present observations with standard chromosome complements of the two species, *Ae. mutica* and *Ae. speltoides*, show that the genotypes examined, which do not promote homoeologous pairing, could not have been the source of the regulation exercised by *5B* in polyploid wheat. Moreover, in low pairing hybrids, derived from the crosses *T. aestivum* tetrasomic *7B* × *Ae. mutica* or *Ae. speltoides*, a bivalent was always formed between the two *7B* chromosomes present⁴. Thus, the restriction of pairing in these hybrids applies only to that taking place between homoeologous chromosomes and not to that between full homologues, so that low pairing is not merely due to an asynaptic effect.

There is still no indication of pre-existing genetic variation in the standard complements of diploid relatives of wheat that could have been the source of the *Ph* allele. However, supernumerary chromosomes of *Ae. mutica* and *Ae. speltoides* carry out a genetic activity that limits homoeologous pairing, so resembling that of chromosome *5B*. The incorporation of a critical segment of supernumerary chromosomal material, possibly by translocation, might, therefore, have given rise to the present effect of chromosome *5B* on meiotic pairing.

Arguments based on the absence of meiotic pairing between supernumerary chromosomes and *5B*, and on the induction of allelic variation in supernumerary chromosomal material, can be advanced against this idea. Nevertheless, only these chromosomes have a similar genetic activity to *Ph*. Consequently the question of the origin of the *5B* effect remains open but our present work has added a third possible mode of origin. Further work will be needed to discriminate between

the three potential sources of *Ph* which are (i) the inclusion at the initiation of polyploidy of a standard chromosome—which has not been detected among contemporary diploids—with an activity preventing homoeologous synapsis, (ii) the origin by mutation, in the polyploid, of an allele preventing homoeologous synapsis and (iii) the incorporation in *5B* of supernumerary chromosome material.

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Critical By-products in the Synthesis of Polychlorobiphenyls

PURE samples of polychlorobiphenyls are desirable for toxicity testing in preference to the randomly substituted products¹ of commercial synthesis. Substrates required (by G. Denton) for specific tests with the American hard-shelled clam *Macra mercenaria* were obtained by chlorination of N,N-diacetylbenzidine². This method has the advantage that the starting material can be obtained in a pure state and, following chlorination in acetic acid solution, the derivative (Fig. 1; X,Y=NHAc, Z=H) can be diazotized and reduced to the tetrachlorobiphenyl (Fig. 1; X,Y,Z=H; Fig. 2, peak A) or further chlorinated by the Sandmeyer method to the hexachloro compound (Fig. 1; X,Y=Cl, Z=H; Fig. 2, peak B). The method has been used by a number of groups³, who have not, however, commented on the many by-products formed. Gas chromatography using an electron capture detector revealed eight significant components and seven minor products from the Sandmeyer reaction, while deamination of the same starting material gave two major and three other products (Fig. 2). None of these peaks was detected in laboratory solvents. We have been able to show that these complex mixtures arise from two known side-reactions which have not been detected before in PCB chemistry.

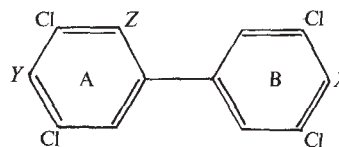


Fig. 1 Outline formula for substrate preparation based on chlorinated N,N-diacetylbenzidine.

In the first place N,N-diacetyl-3,5,3',5'-tetrachlorobenzidine (Fig. 1; X,Y=NHAc, Z=H) is deacetylated to the mono-acetyl compound (Fig. 1; X=NHAc, Y=NH₂, Z=H) in the conditions used for chlorination. This change is probably favoured by relief of strain induced by the *cis*-interactions of two chlorine atoms and the bulkier acetyl amino substituent. In consequence the revealed amino group increases the relative rate of chlorination of ring A. Evidence for this was found when one of the main products of the Sandmeyer reaction was

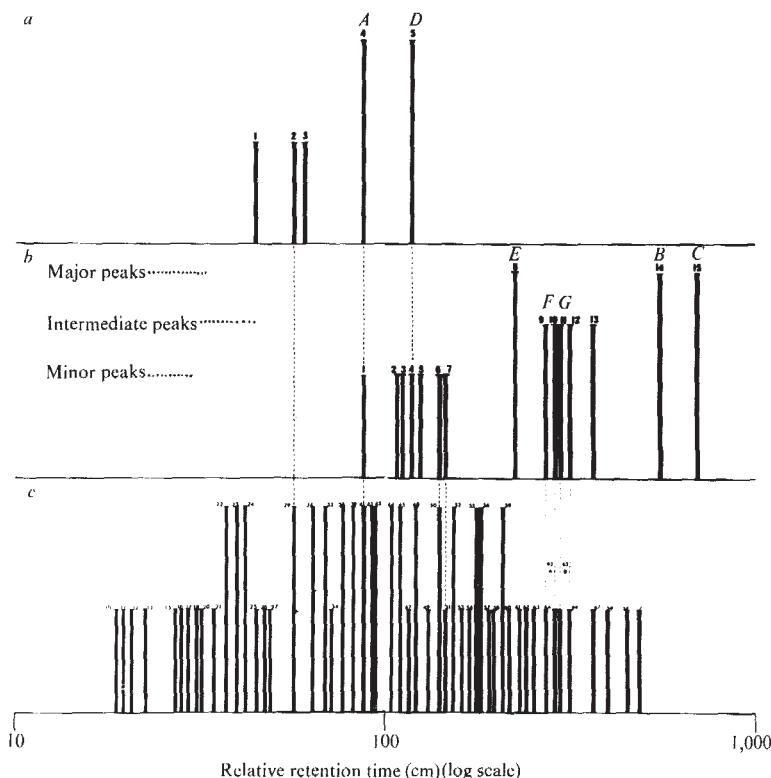


Fig. 2 GC separation of the products of (a) reduction; (b) Sandmeyer reaction with (c) Aroclor 1254 as template—50 foot SCOT column, stationary phase 'Apiezon L' at 190° C.

identified as 2,3,4,5,3',4',5'-heptachlorobiphenyl (Fig. 1; $X, Y, Z = \text{Cl}$; Fig. 2, peak C) by NMR and mass spectroscopy. These methods were also used to identify two other new compounds. Alumina (hexane) chromatography followed by recrystallization (ethanol) was used where preparative gas chromatography was ineffective for the purification of 2,3,5,3',5'-pentachlorobiphenyl (Fig. 1; $X, Y = \text{H}, Z = \text{Cl}$; Fig. 2, peak D) from the reduction, the formation of which is further evidence of excessive chlorination. The isomeric 3,4,5,3',5'-pentachlorobiphenyl (Fig. 1; $X, Z = \text{H}, Y = \text{Cl}$; Fig. 2, peak E) was isolated from the Sandmeyer reaction and clearly arises from competing reduction. This reaction has been demonstrated⁴ during Sandmeyer reactions of the analogous 2,4,6-trichlorobenzene diazonium derivatives and under the conditions of the Van Roosmalen procedure² both nitrogen functions (of I) may be removed in this way. Thus 3,5,3',5'-tetrachlorobiphenyl (peak A), a major product of reduction, was also detected (by GC) as a minor component of the Sandmeyer synthesis, where the greater number of products is to be expected, since competing reduction of one or both diazo functions in symmetrically or unsymmetrically chlorinated precursors is possible. By using the GC of Aroclor 1,254 as a template we have been able to identify other minor components in these mixtures from their retention indices¹; for example 2,3,5,3',4',5'-hexachlorobiphenyl (Fig. 1; $X, Z = \text{Cl}; Y = \text{H}$; Fig. 2, peak F) and 2,3,4,5,3',5'-hexachlorobiphenyl (Fig. 1; $X = \text{H}, Y, Z = \text{Cl}$; Fig. 2, peak G) were identified as reduction products during the Sandmeyer reaction. Full details of this correlation and of the spectra of the major components will be published elsewhere.

It is possible that the extent of bi-product formation can be controlled, but not eliminated entirely, by adopting the conditions used⁵ for hindered anilines.

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Eggshell Thinning and DDE

Blus, Gish, Belisle and Prouty allege that DDE causes eggshell thinning in brown pelicans and that the relationship is logarithmic¹. In support of their conclusion that a cause and effect relationship between DDE and shell thinning exists, they offer as evidence Wiemeyer and Porter's² work with kestrels. A critical review, however, shows that Wiemeyer and Porter have not shown DDE causes shell thinning; on the contrary, the thinnest eggshells in both years of that study were laid by the control group. The control birds laid eggs with shells ranging in thickness from 130 μm –210 μm in both years, while the DDE-treated birds laid eggs ranging in thickness from 165 μm –203 μm and 153 μm –185 μm for the respective years of the study. Blus *et al.* also state that DDE levels reported in Wiemeyer and Porter's experimental kestrels approximate environmental levels found in wild falcons. Such a claim is not borne out by Cade *et al.*³ who have performed extensive tissue analysis, and a comparison shows that the levels in the experimental kestrels exceed levels accumulated in wild falcons by a factor of about two. Despite this, Wiemeyer and Porter only report mean shell thinning of 9.7%, considerably less than the 17% and 35% shell thinning reported by Blus *et al.* in the South Carolina and California brown pelican colonies. To support their conclusions, the authors state that concentrations of residues in the female determine shell thickness, a claim which is unreferenced, largely hypothetical, and without consideration of contradictory experimental evidence.

Blus *et al.* draw their conclusions from statistical analysis of egg residues and eggshells collected over two years from three populations and two subspecies of brown pelicans and combine these to form one bivariate population. The authors assume,

therefore, that no environmental, behavioural, genetic, or physiological differences exist between years, populations or subspecies which could cause differential variation in shell thickness quite independent of the alleged effects of DDE, even though it has been repeatedly shown in poultry that a large variety of factors, intrinsic and extrinsic in nature, can cause eggshell variation⁴. As far as applying regression analysis or correlation to such a composite group, Walker and Lev⁵ have clearly established the limitations of such analyses when they state: "Sometimes two groups with widely separated means are thrown together to form one bivariate distribution. The correlations obtained from a composite group of this sort are spurious and meaningless. . . . When the groups have different means on one or both variables, the effect of combining them may be to produce a correlation coefficient larger than the correlation in the separate groups . . . or smaller, or even different in sign." It follows that regression analysis would be similarly biased. If the hypothesis of DDE caused eggshell thinning is true, particularly at the low levels Blus *et al.* claim, it must exist within a population; however, visual examination of Fig. 1 (ref. 1) suggests that it does not.

The authors claim that analysis of covariance revealed no significant differences among slopes of the three populations and that variation in eggshell thickness may therefore be explained by a common regression. This faulty logic cannot pass unrefuted. The regression slopes of each population may well be related; however, no evidence is presented to show they are related to the common regression which is necessary if the common regression is used to explain the variation in each population as the authors have done. Additionally, the authors have used Pearson's product-moment correlation coefficient in an attempt to further elucidate the DDE-eggshell relation, a correlation inappropriate to their data since it does not exhibit a bivariate normal distribution.

It is clear that the statistical relationship proffered to show a cause and effect relationship is a function of grouping unrelated populations and subspecies, and no evidence is presented to eliminate the myriad of other factors which could explain the inter-temporal, inter-population or inter-subspecies difference.

Finally, no consideration is made for bias which may be inherent in a collection of eggs gathered by oologists and museum collectors before 1947 who would probably favour larger, thicker eggs and who would certainly exclude fractured eggs. This may well explain the apparent thinning in the scientific collection of 1969 and 1970 in brown pelican eggs from South Carolina and Florida.

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¹ Blus, L. J., Gish, C. D., Belisle, A. A., and Prouty, R. M., *Nature*, **235**, 376 (1972).

² Wiemeyer, S. N., and Porter, R. D., *Nature*, **227**, 737 (1970).

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⁴ James, P. E., and Retzer, H. J., *Poultry Sci.*, **46**, 1200 (1967).

⁵ Walker, H. M., and Lev, J., *Elementary Statistical Methods* (Holt, Rinehart and Winston, New York, 1958).

Switzer, Wolfe and Lewin have chosen to ignore obvious evidence in their criticism of our study¹ of the thinning of eggshells of captive American kestrels given a low dietary level of DDE and of data relating to it. They first question the

validity of our experimental results by trying to show that eggshell thinning did not occur in our DDE-dosed hawks because the thinnest eggshells in both years of our study were laid by the undosed group. They completely ignore the shell thickness means and standard errors which are the most reliable statistics for valid evaluation of the data. They also ignore the fact that the experimental design called for a comparison of the changes from one year to the next in thickness of eggshells of individual birds within treatment groups, rather than a gross comparison each year between dosed and undosed groups. Mean eggshell thickness of the undosed birds was, in fact, greater than that of the dosed birds both years, but especially so after a year on dosage. We found a highly significant decline ($P < 0.001$) in the average eggshell thickness of our DDE-dosed kestrels following one year on dosage, while there was no significant decline ($P > 0.05$) in the average eggshell thickness of the undosed group during the same time period. One female in the undosed group laid abnormally thin-shelled eggs during both years of the experiment. We do not know the cause, although it could be an inherited or physiological characteristic of this particular bird. The shell thickness of the next thinnest egg from the undosed group was 0.173 mm in 1968 and 0.160 mm in 1969. We wish to emphasize that there was a decline in shell thickness for every female in the dosed group following one year on dosage, whereas the shell thickness of eggs of one-half of the females in the undosed group either remained unchanged or increased during the same period, changes attributable to random variation.

Switzer *et al.* next question the claim by Blus *et al.*² that DDE levels in our dosed kestrels are similar environmental levels found in wild falcons. In making this criticism, they have ignored several important papers that support this claim. We cited two such papers^{3,4} in our article. One recent paper by Cade *et al.*⁵ reports on DDE residues in 44 peregrine falcon eggs from Alaska, collected in recent years. Close examination of Fig. 1 of that paper shows that about one-half of these peregrine eggs contained DDE residues that were within the range of residues in our kestrel eggs following one year on dosage. We fail to understand why Switzer *et al.* cite only the earlier paper by Cade *et al.*⁶ in which the residues in only two peregrine eggs were reported, while ignoring papers in which the residues in larger numbers of peregrine eggs were reported. We have cited three such papers here which report on residues in a total of 78 peregrine eggs.

Finally, Switzer *et al.* point out the smaller percentage of eggshell thinning in our kestrels compared with that found by Blus *et al.*² in the eggshells of the brown pelican. Blus *et al.*² have discussed the differences in eggshell thinning among various species of birds with relation to given amounts of DDE in the egg. Some species appear to be much less subject to shell thinning than others, which could serve to explain the difference in amount of eggshell thinning between our captive dosed kestrels and wild brown pelicans.

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⁶ Cade, T. J., White, C. M., and Hough, J. R., *Condor*, **70**, 170 (1968).

Reply to Hazeltine

HAZELTINE states, "The conclusion that DDE is the cause of thin brown pelican or peregrine eggs is well established in the popular press and the scientific literature but the underlying data are just now becoming available to test the conclusion. These underlying data do not support such a conclusion . . ." He evidently has in his possession a copy of a paper in press from our laboratory, which includes residue data, because he has made his own calculations for some of the figures from Anacapa Island. He has not mentioned, however, that the paper includes residue data and thickness measurements of 199 individual brown pelican eggs. The statistical analyses of the relationships among the variables show (1) 81% of the deviation in shell thickness from the expected can be accounted for regression on DDE, (2) the distribution of the residuals about the regression line is Gaussian throughout the range of DDE values, from very low to exceptionally high, indicating that there is no reason to believe that other pollutants or environmental factors are affecting the shell thickness changes, (3) none of the other pollutants examined can be related to the changes in shell thickness.

Using analysis of variance, this regression can be shown to be highly significant ($F=754_{df1,197}$, $P<0.001$). Hazeltine has ignored these data in order to advance his own arguments, yet goes on to say, "There is no place in science for suppressed conflicting data, or an end justifies the means philosophy. Scientists can be responsible agents for change only when they consider and present all the available data which bear upon their conclusion."

Hazeltine has obviously not understood the data supplied to him by the California Department of Fish and Game. Five of the eggs discussed in Table 1 were evidently fresh and not incubated. The weight of yolk in these ranges from 13.6 to 17.5 g, a relatively narrow span. The percentage lipid in these samples is also comparatively constant, from a low of 21.8 to a high of 26.9%. The remaining eggs had evidently been incubated and the weight of the "yolk" increases dramatically. Evidently it is not the yolk that is weighed but the complex of yolk with an embryo. His conclusion that "lipid levels in the yolk dropped nearly ten-fold during incubation (26.9 to 2.8%)" cannot therefore be considered valid. As the weight of the entire egg contents is not given, it is not possible to calculate whole egg residues of DDE. What he has evidently done is to consider that the yolk or the yolk plus embryo is equivalent to whole egg residues on a parts per million basis. A p.p.m. concentration of the whole yolk, however, is very different from the p.p.m. concentrations of the entire egg content, yet he goes on to conclude that "as the yolk is incubated, residues are subject to metabolism along with the other yolk contents" and "DDE residues are metabolized as brown pelican eggs are incubated". This conclusion can hardly be extrapolated from the few data presented. At best he might have compared total egg contents in micrograms but, as only ten eggs were involved with different amounts of DDE to begin with, how can he make any conclusions about metabolism during incubation? As the residues are expressed in terms of their concentrations in two very different kinds of tissues, yolk, or the embryo with the remnants of the yolk, they can hardly be used for a correlation with thickness.

Hazeltine's initial disagreement with the result of the paper by Blus *et al.*² is that "none of the separate colonies shows a clear trend in itself". As a particular colony may show a comparatively restricted range in residue distribution, small samples should not be expected to show relationships which become apparent only when DDE concentrations range from 0 to 3,000 p.p.m. and when shell thickness ranges from normal to a layer which is barely more than the membrane. Yet, whenever a larger sample is available, the trends emerge. His sentence, "If this overall correlation is meaningful, each colony should show a similar trend in itself, which is not the case," is false because the sample sizes of individual colonies are

relatively small, showing a relatively restricted range of residue levels and shell thickness values.

Blus *et al.*² give a regression coefficient which is different from 0 at the 0.01 level of significance. There is therefore no way that the confidence interval can include 0. Perhaps the drawing given in the paper by Blus *et al.* is misleading, but a significance level of this magnitude does not suggest "extremely variable supporting values for a regression" as Hazeltine states.

He quotes me as stating that "non-parametric statistics are called for". This is a misinterpretation of my remarks. A number of statistical languages, including the analysis of variance of regression, can adequately describe these data. Hazeltine states, "Using logarithms for residue levels shows that residues are not normally distributed around a mean value." Transformation of residue data, including many of these pelican data, to logarithms frequently does convert them to a distribution that sufficiently approximates normality. As his statement stands, it is meaningless. How can the mere transformation of data to their logarithms in itself show the mathematical nature of the distribution without additional tests? We have looked at the goodness of fit of a number of pollutant distributions, including those in the pelican samples, with various mathematical distributions. In some cases the log-normal provides an excellent fit and Hazeltine's statement that the residues are not normally distributed around the mean value is false. In several other cases the gamma distribution more adequately describes the observed distribution of pollutants.

The short paragraph on the peregrine falcon hardly does justice to the important questions involved. Many statements are made without support and are incorrect.

One wonders just which data were "suppressed" and which were "conflicting". One begins to suspect intrigue and conspiracy, yet he has carefully avoided the consideration and presentation of "all the available data". I look forward to discussing these questions at much greater length at a meeting in London to be held on November 21, 1972, sponsored by the British Ornithologist Union, the British Trust for Ornithology and the Royal Society for the Protection of Birds, devoted to the question of pollutant effects upon bird populations.

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¹ Hazeltine, W., *Nature*, **239**, 410 (1972).

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Further Analysis of the Logarithmic Relationship of DDE Residues to Eggshell Thinning

HAZELTINE¹ disputes our conclusion^{2,3} that DDE is the agent responsible for all or most of the eggshell thinning observed in the brown pelican. We have examined the criticisms and found them to be without substance. We will now refute Hazeltine's rebuttal of our paper.

In the first of his points of disagreement Hazeltine states that if the overall relationships between DDE and shell thinning mean anything, "... each colony should show a similar trend in itself. . . . None of the separate colonies shows a clear trend in itself". This criticism is erroneous. In the comparison of eggshell thickness to DDE residues by States, the regressions

for the South Carolina and California data are not significant ($P > 0.05$), but a significant relationship ($P < 0.01$) was calculated in the Florida data (Table 1), which Hazeltine ignores in his analysis.

A non-significant relationship between eggshell thickness and DDE residues within a single colony or several colonies in a local area does not invalidate our conclusions. Within each colony of pelicans, both residues and eggshell thicknesses tend to be similar. The California data are from a single colony with extremely high DDE residues, and, as we have shown², the percentage change in thickness was greater per unit of DDE when the concentration of DDE was lower. Thus, the changes in thickness per unit of DDE is very low in the California series.

Table 1 Regression Equations and Percentage of Variability in the Percentage of Pre-1947 Eggshell Thickness accounted for by DDE Egg Residues, Egg Basis

State	No. of eggs	% of variability	Regression equation
Fresh wet weight			
South Carolina	21	4.0	$\hat{Y} = 89.389 - 4.649 \log_{10} X$
California	10	4.8	$\hat{Y} = 81.451 - 8.812 \log_{10} X$
Florida	49	22.1 *	$\hat{Y} = 95.389 - 9.925 \log_{10} X$
All States	80	64.0 *	$\hat{Y} = 95.787 - 15.689 \log_{10} X$
Fresh lipid weight			
South Carolina	21	4.0	$\hat{Y} = 96.263 - 5.431 \log_{10} X$
California	10	4.0	$\hat{Y} = 94.720 - 9.125 \log_{10} X$
Florida	49	23.0 *	$\hat{Y} = 110.959 - 11.479 \log_{10} X$
All States	80	64.0 *	$\hat{Y} = 116.160 - 15.235 \log_{10} X$

* $P < 0.01$.

In the two South Carolina colonies, the residues lie within a narrow range. As most of the residues were similar within a local population, the regressions for California and South Carolina were not statistically significant. In Florida where nine colonies were involved and the residues covered a wider relative range, a significant relationship was present. The smaller DDE residues in Florida eggs also tended to be related to a greater relative shell thinning and so enhanced the likelihood of a significant statistical relationship. The analysis of covariance revealed no significant difference in either parallelism between the regression lines or between the adjusted treatment means of data from the three States; it is therefore valid to combine the data for analysis.

Risebrough⁴ warned against using residue data from a local area in assessing biological effects induced by the residues. Some investigators^{5,6} have overcome this problem by using colony means, a method that seemingly is as valid as using the individual egg as the sampling unit. When we used the colony means as the sampling unit, we found a significant regression (Table 2).

Table 2 Regression Equations and Percentage of Variability in the Percentage of Pre-1947 Eggshell Thickness accounted for by DDE Egg Residues, Colony Basis

No. of colonies	Percentage of variability	Regression equation
Fresh wet weight		
12	92.2 *	$\hat{Y} = 96.410 - 16.509 \log_{10} X$
Fresh lipid weight		
12	90.3 *	$\hat{Y} = 117.713 - 15.964 \log_{10} X$

* $P < 0.01$.

We believe our statistical procedures and conclusions to be entirely valid. We have had competent statistical advice throughout from E. James Koch, a senior statistician with the United States Department of Agriculture, and Robert G. Heath, a biometrician at our centre. One of us (C. D. G.) has had advanced training in statistics.

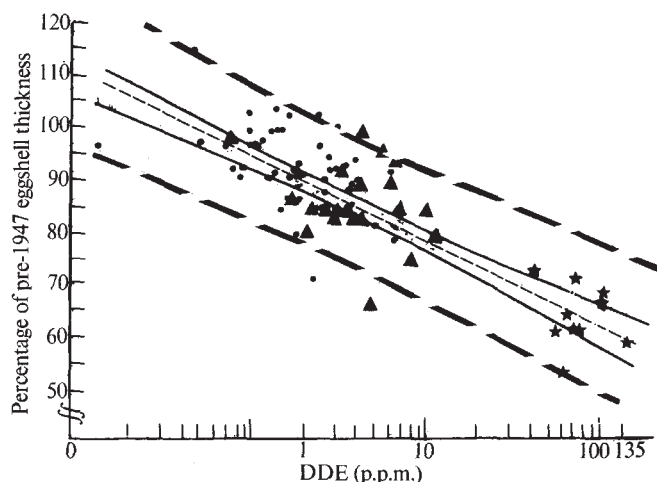


Fig. 1 Association of DDE residues in 80 pelican eggs from Florida (●), South Carolina (▲) and California (*) with the percentage of pre-1947 eggshell thickness. The regression line (—) is shown together with the 95% confidence limits for both the regression line (---) and the individual $\hat{Y}$ values (---). $\hat{Y} = 95.787 - 15.689 \log_{10} X$; $r = -0.80$ ($P < 0.01$).

In his second criticism, Hazeltine indicated that the wide confidence limits in our Fig. 1 suggested an excessive variability. The data points on this figure are correct; however, recalculation of the confidence limits did show an arithmetical error. The 95% confidence limits for both the regression line and individual $\hat{Y}$ values were recalculated (Fig. 1). Both sets of confidence limits are in fact much narrower than those previously reported.

In Hazeltine's third point of criticism, he states, "... whole egg analysis is inappropriate for incubated eggs because the residues are found in the yolk, and during incubation yolk contents including residues are subject to metabolic changes". This conclusion is also incorrect and appears to have resulted from a misinterpretation of raw data of others, plus a lack of knowledge of the pertinent literature.

In experimental studies with chicken eggs injected with (DDT-¹⁴C) prior to incubation, virtually all of the injected DDT was present in the egg as DDT or its metabolites by the nineteenth day of incubation^{7,8}. In eggs injected with 1 mg of DDE prior to incubation, DDE and a relatively small amount of 4,4-dichlorobenzophenone were found in the recently hatched chick⁷. The authors concluded that DDE is not readily metabolized in the egg. This suggests that when DDE enters the egg of the brown pelican, it remains in the egg and very little is metabolized to other compounds. Some of the DDT would be expected to be metabolized to DDE as this has been found in injected eggs⁷, but most of the exposure of pelicans is to DDE and this conversion of DDT to DDE would not be expected to interfere with the relationship of DDE residues to eggshell thinning.

Hazeltine's misinterpretation of raw data was explained by James O. Keith in a letter to Hazeltine. Keith has intimate knowledge of these nine eggs⁹, and he states that all of the eggs were freshly laid. The eggs termed embryonated by Hazeltine were ones in which the yolk burst when frozen. The California Fish and Game Department ordinarily analyse whole yolk. In the four eggs in which the yolk burst, they analysed yolk plus some albumen as they were unable to completely separate yolk and albumen. Thus, Hazeltine's residues on a whole yolk basis are based on whole yolk in five eggs and yolk plus some albumen in four eggs. As a result, Hazeltine has no basis for determining that yolk lipids and DDE residues decrease during incubation.

In Hazeltine's fourth point, he stated that "... the use of Pearson's product moment correlation coefficient (r) is not an appropriate method for values which are not bi-variantly normally distributed". This statement is in error. Hazeltine

erroneously interchanges the assumption for a bivariate normal distribution between correlation and regression. Our reason for transforming residues to logarithms was to achieve an essentially linear relationship with the percentage of pre-1947 eggshell thickness.

In regard to the four points Hazeltine attempts to draw from his Table 1, all of these are erroneous because all of the nine eggs were freshly laid, as we described previously. Further definitive relationships between shell thinning and DDE residues on a lipid basis are available from our own study. Residues in eggs can be expressed on a variety of bases. We used the wet weight basis, adjusted for moisture loss, in our previous paper because we believe this method provides the most valid comparisons of analyses made at different laboratories. When all procedures of extraction and analysis are identical, as in our series of brown pelican eggs, a lipid base can also be employed. However, since lipid levels in the egg decrease by about one-third from laying to hatching¹², an adjustment must be made for this loss. We have made this adjustment for our eggs on the basis of percentage lipids in freshly laid brown pelican eggs. By adjusting the egg residues to a fresh lipid weight, there were no differences in the statistical results when compared to those obtained by using fresh wet weight. This was true whether the sampling unit was the individual egg (Table 1) or the colony mean (Table 2).

Some additional errors in Hazeltine's presentation should also be noted. Hazeltine appears confused when speaking of Risebrough's California brown pelican data. He, like Risebrough⁴, also found a significant negative relationship between the DDE egg residues (lipid basis) and shell thickness using Risebrough's data. But on the basis of a much smaller sample, he indicates that there is a positive relationship between DDE egg residues (lipid basis) and shell thinning in the California brown pelican. In our opinion, Hazeltine failed to recognize that the negative correlation that he found using Risebrough's data essentially negates all of his arguments.

Since we were further misquoted in regard to the work of Cade and his colleagues¹³, it should be made clear that we merely pointed out that DDE residues in captive sparrow hawks fed DDE and undergoing reproductive difficulties and shell thinning¹⁴ were similar to the residues found in wild peregrines undergoing reproductive difficulties and shell thinning. Cade presents convincing evidence of the relationship of DDE to eggshell thinning in the peregrine at a time when reproductive success was subnormal.

We know of no suppressed conflicting data. We have presented all of our available evidence, and we stand behind our original methods and our conclusions that DDE has significantly thinned eggshells of brown pelicans.

Comments by B. C. Switzer and his colleagues in an earlier letter to *Nature* included only a few points that are not covered above. Switzer *et al.* mistakenly stated that we claimed that concentration of DDE residues in the female determines eggshell thickness. We in fact said that the amount of DDE in the egg is taken as an index to the concentration of residues in the female¹⁵⁻¹⁷, the physiological processes of which determine shell thickness. We wished to make it clear that the residues in the egg did not directly affect shell thickness; this had to be determined earlier. If shell thickness is not determined by the physiological processes of the female, what can determine it? Switzer and his colleagues did not document the source of the contradictory experimental evidence they say exists.

They further erroneously stated that we claimed a cause-and-effect relationship on the basis of our pelican data. We claimed a cause-and-effect relationship between DDE and eggshell thinning on the basis of experimental data^{14,18,19}. The pelican data come as near to a perfect field relationship between a pollutant and an adverse biological effect as we can expect in pollution studies.

Switzer further suggests that early museum eggs were biased toward thicker eggs. The evidence we have encountered

indicates that this is unlikely. We have noted runt eggs and depredated eggs in museum collections. There were probably few thin shelled eggs available. Even more conclusive, however, is the fact that the striking changes in shell thickness in the 1940s have been entirely from museum series^{5,20}. As a further point, direct use of contemporary eggshell thickness in place of percentage of pre-1947 thickness also showed a significant negative relationship with DDE egg residues³. Significant differences in thickness between colonies were also found in 1969²¹; thus, the evidence for shell thinning does not depend solely upon comparisons with pre-1947 measurements.

The evidence from our field study, taken with the evidence from many other studies, is scientifically sound and it would seem virtually impossible that the relationship between DDE and shell thinning is spurious. Objective scientists cannot completely rule out the possibility that some other pollutant or some factor closely associated with DDE may have induced the eggshell thinning recorded for the brown pelican; however, such a possibility seems exceedingly remote.

We thank E. James Koch, Robert G. Heath, and Lucille F. Stickel for their invaluable advice.

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The following amendment by Dr Hazeltine was submitted too late for publication in his previous letter.

Recently disclosed errors in the original laboratory reports invalidate the conclusions of ten-fold lipid and DDE residue decline with incubation. The increasing lipid basis DDE residue correlation to increasing shell thickness is still valid and refutes the contention of cause and effect between egg residue and shell thickness. This lipid basis conclusion refutes whole egg weight DDE residue correlations as well.

BOOK REVIEWS

Psychology on a Behaviourist Basis

Woodworth and Schlosberg's Experimental Psychology. By J. W. Kling and Lorrin A. Riggs and seventeen contributors. Revised edition. Pp. xiv+1279. (Methuen: London, February 1972.) £9.50.

In 1938 Woodworth published the first edition of *Experimental Psychology*. It covered the whole of the subject, was written with enthusiasm and vigour and remained much the best textbook in the field until the early 1950s. In 1954 Woodworth and Schlosberg published a completely revised edition which was again comprehensive in coverage and proved to be a most useful undergraduate text although by that time other good texts at an advanced undergraduate level were beginning to appear. Woodworth's text has gone the way of Winton and Bayliss and the present edition contains twenty-one chapters in the writing of which nineteen different authors have played a part. Good though some of the individual chapters are, the work as a whole no longer has the coherence of the earlier editions. Nor does it have the feeling of excitement that Woodworth himself conveyed. Indeed some of the chapters combine the turgidity of American scientific writing with the monotony of scientific American prose.

The editors themselves state that "we make no claim for completeness of coverage of this book . . . we choose to cover in depth the topics most thoroughly explored with the idea that the methods and principles involved will be found common to areas remaining for future exploration". Unfortunately most of the methods and principles that appear in the book were current in the 1950s or earlier. Although experimental techniques have not changed drastically since then, ways of thinking about mental processes have changed more in the last twenty years than in the whole of the preceding history of the subject as far back as the onset of behaviourism as introduced by Pavlov, Thorndike and Ebbinghaus.

The conceptual revolution through which psychology is at present passing results largely from the advent of the

digital computer which makes it possible for the first time to propose and test complex theories of the way in which information is processed by the human brain. Complex cognitive operations have been shown to pervade every aspect of human activity including the performance of deceptively simple tasks such as learning lists of nonsense syllables. The behaviour of man and animals can neither be explained in traditional stimulus-response terms nor in terms of the mode of operation of individual nerve fibres. An understanding of the mechanisms underlying behaviour depends upon developing a formalism in which to characterize knowledge and the ways in which it can be deployed to interpret incoming stimuli. In the last ten years we have begun to develop a set of concepts in terms of which it is possible to understand how knowledge is represented and used. These concepts and the new way of thinking embodied in them have arisen at least in part from developments in artificial intelligence and from the success of workers in linguistics in their attempt to provide a formal characterization of syntax. There is almost no mention in this volume of the new theoretical tools now at our disposal; it is rather as though a textbook of physics had appeared in 1930 that made no mention of quantum theory.

Perhaps part of the reason for the lack of excitement in this book is that many of the issues that are discussed and much of the theoretical framework used are of little relevance to current work. Many of the most exciting areas of recent experimental work are scarcely mentioned. There is, for example, almost no reference to work on cognition, psycholinguistics or object recognition. Moreover, almost a third of the book is devoted to neurophysiology and, worthy though these chapters are, in many instances little attempt is made to relate neurophysiological findings to behaviour. The chapter by Alpern on eye movements, for example, is an exceptionally clear statement of the current state of physiological know-

ledge but it contains almost no discussion of the functional role of eye movements in vision.

There has been a tendency amongst some psychologists to assume that any aspect of behaviour that can be measured must be interesting. This tendency has been fostered partly by the anti-theoretical bias of workers such as Skinner, who places more emphasis on the control of behaviour than on the understanding of it, and partly by the lack of an adequate theoretical framework within which to achieve an understanding. In addition there has been a good deal of scholasticism. Behaviour in a given situation is investigated for no other reason than that it can be easily measured in that situation; micro-theories are produced to "explain" the behaviour, curves are fitted with glee, and parametric studies undertaken without giving much thought to whether the theories have any plausibility or relevance outside the specific experimental situations in the context of which they were introduced. Postman's chapter on verbal learning in the present volume is a travesty of this approach and it comes almost as a surprise that he does not get down to discussing how many nonsense syllables can dance on the face of a Gerbrand's tachistoscope. It is not without significance that some of the most interesting work produced by experimental psychologists has been undertaken by men such as Bartlett and Tolman who were not sophisticated enough to understand the details of current theoretical wrangles but who had enough common sense to recognize what was an important problem and what was plausible.

Despite these adverse comments, there are some good things in the present book. Engen gives a remarkably clear account of signal detection theory which, together with control theory, is the only branch of conventional mathematics that has actually proved useful and illuminating when applied to psychological problems. Hochberg looks at visual perception through the eyes of a Gestalt psychologist; he surveys many interesting phenomena and

explains some of them. Bartoshik gives a highly readable summary of the little that is known about taste mechanisms and Riggs gives an elementary but readable introduction to some of the more peripheral aspects of vision.

This book will still be read in fifty years' time—but only by those who are interested in the dying kick of a narrowly based behaviourism.

N. S. SUTHERLAND

Fleas

An Illustrated Catalogue of the Rothschild Collection of Fleas (Siphonaptera) in the British Museum of Natural History. By J. H. E. Hopkins and Miriam Rothschild. Pp. 350+842 text figs. and 30 plates (6 colour). (British Museum: London, 1972.) £25.

THE trustees of the British Museum (Natural History) are to be congratulated on their enterprise and perspicacity in producing the first monograph of an order of insects as extensive as fleas. The fifth volume maintains the excellence of the earlier ones. It deals with one large and taxonomically difficult family, the Leptopsyllidae, and one very small one, the Ancistropsyllidae. The illustrations in this volume bring the total now published in the series to well over 4,000, all of them of high quality. The keys to genera and species are simple and clear and designed for the medical entomologist rather than for the specialist.

An outstanding feature of volume V is the glossary of terms and the morphological studies upon which the definitions and descriptions of the organs are based, a part that seems to owe much to Robert Traub. A number of points of more general interest are discussed. The position of the pleural arch on top of the pleural ridge suggests that it is homologous with the wing-hinge ligament of flying insects, which is further supported by the presence of resilin in the pleural arch. Sections of the pharate adult stage show that the combs of pronotal spines are modified setae. Their work on the histology and morphology of the female reproductive system confirms Jordan's view that the family Hystichopsyllidae was evolved before other recent families of fleas.

It is a pity that the monograph is called an illustrated catalogue, which not only conjures up quite the wrong impression of its contents but successfully conceals its monographic nature and must discourage the purchase of an important addition to every medical and entomological library. The next volume on the Cerophyllidae will be eagerly awaited by epidemiologists and specialists on fleas.

H. E. HINTON

Nuclear Common Sense

Economic and Social Consequences of Nuclear Energy. Edited by Lord Sherfield. Pp. v+91. (Oxford University: London, March 1972.) £1.

THIS little book is, according to the blurb on its cover, part of a series "intended to provide a medium for the discussion of various aspects of the impact of scientific discovery and technological development on society". It consists of six independent chapters, each written by a person who has long been identified with the nuclear speciality he is describing. Professor Robert Spence writes on the science of fission and fusion; Air Chief Marshal Sir Denis Barnett on the technology of nuclear explosives; Sir Stanley Brown on the economics of nuclear power; the late Dr Hans Kronberger on non-power and non-military uses of nuclear energy; the Right Reverend Robert C. Mortimer on the moral aspects; and Lord Ritchie-Calder on the sociological consequences of nuclear energy. Lord Sherfield, who as Roger Makin served as Chairman of the UKAEA, provides a short summary for the volume.

The science and technology in this volume cannot be faulted: the writers are experts. That they are all British means that the viewpoint is British: the reactors are gas-cooled graphite reactors rather than American water reactors; the wartime experience is that of the Maud Committee rather than the Manhattan Project.

Only the moral and sociological chapters can be considered controversial. To an American nuclear technologist who has grown weary over the past years responding to the increasingly shrill attacks of the anti-nuclear activists, these chapters are welcome examples of low-key British commonsense. The good Bishop of Exeter calls for a peace of repentance but accepts the *de facto* peace of mutual terror. Lord Ritchie-Calder speaks of nuclear energy as a relatively "clean" and "safe" source of electricity. These are unusually reasonable positions to be espoused in this day of harsh acrimony and strident accusation.

Only with respect to the disposal of radioactive wastes would I quarrel with Lord Ritchie-Calder. He sees their disposal as the biggest problem of nuclear energy. This may be so, but it is in a sense more of a social than a technological problem. Nuclear wastes can be disposed of in a variety of ways—particularly in surface vaults or in salt mines—that technically are essentially foolproof. But because their radioactivity lingers for such a long time, the wastes do impose on our society a social commitment: an assurance that from now to perpetuity our social institutions retain sufficient stability to

guarantee the continued existence of a cadre that will take care of the wastes. This is one of the heaviest social consequences of nuclear technology. I was disappointed not to find it stated explicitly in the *Economic and Social Consequences of Nuclear Energy*.

ALVIN M. WEINBERG

Colour Blindness

Acquired Colour Vision Deficiencies: First Symposium of the International Research Group on Colour Vision Deficiencies. Ghent, June 1971. Edited by G. Verriest. Pp. iii+230. (Karger: Basle, London and New York, 1972.) £8.15; \$20.75; 74 Sw. francs.

THIS book is a collection of thirty-five papers contributed to the symposium by distinguished authors who, for the most part, are busy clinicians, concerned to detect early, and classify pathologically, conditions in their patients that are associated with acquired colour abnormalities. The tests used must be quick, and simple enough to give definite answers with quite unskilled observers. Like the rashes of measles and scarlatina, such direct observations may be of great diagnostic importance, but they give little information about the underlying physiology—of skin vascularity in the one case, or of colour perception in the other.

Eleven papers are devoted to methods of examination, starting with W. D. Wright, author of the classic *Researches on Normal and Defective Colour Vision*. Most contributors recommend a combination of tests usually including the anomaloscope, the Farnsworth 100-hue test and the Ishihara (or similar) cards for macular investigation, and various forms of perimetry in the periphery. Many modifications of standard equipment are described and recommended.

Seventeen papers describe the results of these tests in a great variety of acquired deficiencies. An initial review of this very complex subject is set out with masterly clarity by Dubois Poulsen. But after reading the next sixteen papers, one cannot but agree with his opening sentence, "In spite of the numerous works which have been devoted to them, acquired dyschromatopsias are still very mysterious." This section is written by clinicians for clinicians, and their careful observations with a battery of tests will go far to enable a very large variety of diseased conditions to be diagnosed early and correctly.

Seven authors contribute to the final section, "The mechanisms of acquired defectiveness of colour vision, and its study by means of special methods."

Our knowledge is so weak as to how the outputs of the three types of cone are organized to produce colour vision that the study "by special methods" of how the mechanism is modified in disease promises to throw new and much-needed light. This promise remains utterly unfulfilled. No special methods are devised, and no light falls.

Yves-le-Grand (as usual) is incisive, lucid, balanced and up-to-date in his account of where we stand in the knowledge of photopigments. But no contributor builds upon this solid foundation, or even asks specifically the simple question "Is this change in colour vision due to a change in the spectral sensitivity of a cone pigment?" Still less are the simple experiments explicitly performed that will answer this.

Thus anyone who had hoped that this book would throw new light on the organization of colour vision will be disappointed, for it is not written for him but for practising clinicians. But if a reader has the time and the analytical invention himself to engage in the "still very mysterious" domain of acquired dyschromatopsias, and will wrest from that confusion some insight into the organization of colour vision, this book describes a great variety of conditions, and may well suggest to the perceptive some promising points of attack.

W. A. H. RUSHTON

Sociology of Science

The Social Contexts of Research. Edited by Saad Z. Nagi and Ronald G. Corwin. Pp. xii+409. (John Wiley: New York and London, August 1972.) £5.65.

THIS is a very successful collection of essays; the editors have been able to achieve a coherence and thoroughness that are not at all common in such multiauthored works. For the area of studies and policies that might be called "the social administration of research", this book can function as a reliable compendium of the best recent thinking.

The editors themselves contribute an introductory "overview" of the topic, usefully summarizing much recent philosophy and sociology of science; and in the last essay they apply the materials of the book to their own field, educational research. The other nine essays include contributions by such well-known authors as Howard N. Vollmer, Don E. Kash, Simon Marcson and Norman W. Storer; together the essays cover every aspect of the description of research as a socially organized, highly differentiated activity, conducted within a variety of institutional contexts.

It is noticeable that the general discussions of research are based on the experience of the natural sciences and their technologies, while particular problems, as those discussed by the editors and by Irwin Deutscher (on false answers to survey questions), come from the human sciences. This slight imbalance probably reflects the difficulty (that may be lessening now) in finding authors to produce a scholarly résumé of work on particular social and moral problems of "hard" science.

To a reader concerned to understand and cope with the multiplicity of difficulties now facing "the research enterprise", the impression finally conveyed by these very competent surveys is one of blandness. For example, there is the problem of the supposed propensity of scientists to prefer to work on "pure" research unless bludgeoned into more socially responsive ways; why should this be so (if it is so)? Vollmer provides an admirable study of the literature, whose conclusion is more or less that the purist preference is one of those habits that students get at university and hold until circumstances force them to change. One knows that there must be more to it than that; but it might well turn out that only the "entrepreneur" interpretation of the independent research scientist can explain the phenomenon fully. On another key problem, inter-disciplinary conflict, N. W. Storer offers a reasonable general survey, but in a footnote engagingly confesses his naïveté about the ferocity of such struggles; while the editors' essay gives a thorough taxonomy of the phenomenon along with good insights about its causes.

The one jarring note in the book comes from the political right, with a tendentious and inexperienced essay "Forbidden Knowledge" by W. Petersen, a vigorous and refreshing denunciation of the left-wing radical critics of science in America. One might say that such discussions belong to a different book; but it could be answered that a book that ignores the politics of the research industry has not really covered its "social context". It is only from the texts that Petersen quotes disapprovingly that one is reminded that there are a variety of problems associated with a military involvement of university research; that the market and institutional forces shaping research and development do not work so well as to preclude serious discussion of misdirected technology; and that there is still some idealism, doubtless confused and perhaps misguided as well, about something called Science that is distinct from Research.

But these criticisms on the deeper problems of science policy should not detract from the real value of the book for the limited range of problems to which it is devoted. J. R. RAVETZ

Photochemistry of Smog

Chemical Reactions in Urban Atmospheres. Edited by Charles S. Tuesday. (Proceedings of the Symposium held at General Motors Research Laboratories, Warren, Michigan, 1969.) Pp. xiv+287. (American Elsevier: New York, Amsterdam and Barking, December 1971.) Dfl. 60; \$17.75.

THIS volume is likely to be of interest to anyone who wishes to understand the thermal and photochemical reactions which are responsible for the production in the atmosphere of contaminants which constitute "photochemical smog", for it contains eleven papers concerned with various aspects of this problem each followed by brief symposium discussion contributions. Many of the papers give mechanisms with rate constants or relative efficiencies of reactivity for elementary reactions which are suggested as being of possible importance in producing atmospheric pollution. The experimental conditions used include simulated atmospheres as well as conventional gas phase, photochemical and thermal reactors. Although much of the discussion is speculative the kind of experimental evidence available to test the various theories is well illustrated in this volume.

The more applied articles are a discussion of the role of singlet molecular oxygen in the chemistry of urban atmospheres with particular reference to the Los Angeles Basin, a paper entitled hydrocarbon reactivities and nitric oxide conversion in real atmospheres and an analysis of photochemical reactions involving gaseous contaminants of urban atmospheres that result in the formation of aerosols as studied in a large irradiation chamber. In this last paper the problems associated with studies using simulated atmospheres are discussed. Chapters dealing with thermal and photochemical reactions of atmospheric pollutants include those concerned with reactions of sulphur dioxide and the methyl radical-sulphur dioxide reaction. The reactions of oxides of nitrogen receive considerable attention with further articles on the reaction of nitrogen dioxide with olefins and aldehyde-olefin interaction in nitric oxide photosensitized oxidation of aliphatic olefins. The remaining articles are kinetic studies of the photolysis and photo-oxidation of alkyl nitrites, formaldehyde and carbon disulphide in the gas phase together with a report of a very interesting study, using fast flow and static methods, of the reaction of O(³P) with acetaldehyde, propionaldehyde and acrolein, all of which are known pollutants present in photochemical smog.

All the papers are of high standard and are well presented. The factual information given concerning the

mechanism of photochemical and thermal reactions is extensive. Although this volume alone illustrates that present understanding of the reaction mechanisms involved in the formation of atmospheric pollution is still in its infancy, those interested in photochemical smog or the gas phase reactions of atmospheric pollutants will find this a rewarding book to consult.

F. WILKINSON

Harvey Interpreted

William Harvey and the Circulation of Blood. By Gweneth Witteridge. Pp. xiii+269+8 plates. (Macdonald: London; Elsevier: New York, April 1971.) £4.

In recent years Harveian scholarship has flourished at all levels. For the general reader excellent brief surveys have been produced by Keele and Franklin, while Keynes has written a definitive biography and Pagel a brilliant analysis of Harvey's biological philosophy. Mrs Witteridge has already made a substantial contribution to this enterprise with two excellent editions of Harvey's unpublished writings. This book is an interpretative study based on many years of minute investigation of Harvey's manuscripts and books. Few authors have been better equipped to pronounce on Harvey's great achievements.

Mrs Witteridge has strong views, making for a highly distinctive contribution. On every issue determined judgments are expressed, often if not usually running counter to prevailing trends among students of Harvey. The author concentrates on a developmental account of Harvey's ideas on circulation, the topic which will appeal most to readers. His work on embryology is considered only in relation to circulation. Thus attempts at an assessment of Harvey's general scientific outlook are made without extensive reference to his most extensive published work. Harvey is presented unambiguously as an experimental physiologist of the modern type operating within a mental framework which had little regard for authority or philosophical preconceptions. Accordingly his debt to the past was limited and selective. Like the author, Harvey is thought to have had little regard for Cesalpino or other speculative writers, while taking his inspiration from such empiricists as Columbo. Of precursors, only Columbo is discussed in detail, while others are dismissed in a cursory manner.

The strongest section of this book is an accurate account of the unfolding of Harvey's views on the movement of blood. No other author has equalled this precise yet detailed description. On

the mutations of Harvey's ideas subsequent to the discovery of circulation, the author is less convincing and not particularly successful in explaining Harvey's dilemmas in terms of his empirical investigations and laboratory experience.

This otherwise scholarly book has one grave defect. Citations are given in a most inconsistent manner. In some cases footnotes are elaborate; in others page numbers are given in the text, causing slight ambiguity; while in other cases references are entirely omitted. Nevertheless Mrs Witteridge has produced a stimulating interpretative work, which will undoubtedly appeal to a wide audience of scientists and historians. But the reader should then return to Harvey to consider whether the methodological interpretation has been dictated by evidence, or staunch adherence to prevailing opinions about the nature of modern experimental science.

C. WEBSTER

Immunology Made Clear

Antigens, Lymphoid Cells and the Immune Response. By G. J. V. Nossal and G. L. Ada. (Immunology: an International Series of Monographs and Treatises.) Pp. xix+324. (Academic: New York and London, April 1971.) \$17.50; £8.15.

ALTHOUGH a few scientists have expressed the view that immunology is played out in the sense that all the really great discoveries to be made have been made, this is a field that continues to be very exciting, with hardly a dull moment; and, perversely, it is still advancing at breathtaking speed. It is not at all surprising that most practising immunologists take good care not to be lured into writing a book: they are far too busy and a book is likely to be out of date soon after publication. As a result, postgraduate students and research workers have to rely to a great extent on the numerous proceedings of specialized conferences or on edited monographs written by a plethora of contributors. Such books tend to be bitty, to say the least, and they often give a far from balanced, let alone a unified, view of the field under discussion.

Immunologists and immunologists in the making therefore have reason to be grateful to G. J. V. Nossal and G. L. Ada for writing an integrated book on a topic that cuts across many frontiers. The main theme is concerned with the way(s) different antigens impinge on the immunological apparatus in terms of localization, antibody formation and tolerance induction, and this in turn requires an assessment of the anatomy and function of the tissues and cells that participate in the immunological res-

ponse. Whilst I regret the authors' decision not to cover delayed-type hypersensitivity and the allograft reaction—an omission which sometimes weakens the universality of the conclusions drawn and limits the argument somewhat arbitrarily—Nossal and Ada have produced a book which is characteristically lucid and immensely readable despite the complex and sometimes contradictory experimental evidence. Notwithstanding the presence of innumerable trees of all shapes and sizes, the reader is given a very fair view of the wood itself, thanks largely to the grasp the authors have of their material and partly to the excellent little summaries at the end of each chapter. If pride of place is, at times, given to their own work and that of their colleagues at the Walter and Eliza Hall Institute no one will carp at this, for they have made many vital contributions to this field.

In spite of the enormous amount of work done on antigen localization in the last decade it comes as something of a shock to realize how little we know to this day of the actual role played by antigens in both antibody formation and tolerance induction. Histocompatibility antigens apart, most workers use either serum proteins (such as BSA or HGG), *Salmonella* flagellin or sheep red blood cells. Even within this limited repertoire some important differences have been described, and one of the messages coming across clearly is that different antigens may be handled and processed differently and that it is unwarranted to draw sweeping conclusions from the study of a single antigen. Another message is that, by and large, modern immunology sustains the clonal selection hypothesis, even though it may be true that the really critical experiment has not yet been performed (and for technical reasons, perhaps never will be, though the very recent work of B. A. Askonas and A. R. Williamson on antibody-producing cell clones and their senescence may have gone some way towards it (*Nature*, 238, 337; 1972)). How appropriate, then, that the book should be dedicated to Sir Macfarlane Burnet.

This book, which should be essential reading for every serious student of immunology, is unfortunately very expensive—more a function of its high quality paper (and perhaps the publisher involved?) than the number of its illustrations. The chapter summaries are most useful, and the arguments are well sustained by full references. Proof-reading has been efficient and there are few howlers, but I enjoyed the statement that "it is confidentially expected that the numerous gaps in Table 11.1 . . . will shortly be filled. . . ." Isn't that taking confidentiality a little too far, Gus?

LESLIE BRENT

CORRESPONDENCE

Nitrites in Trouble

SIR,—In the recent report by your Washington Correspondent (*Nature*, 239, 63; 1972) on the current arguments concerning the permissibility of nitrite as a food additive in the USA, there are several misrepresentations of fact which we feel should be clarified. Further, the opinions expressed in some of the statements have not been adequately substantiated in our opinion by experimental results.

The contention that nitrite is permitted as a curing agent but not as a preservative is a *non sequitur* since by definition the act of curing is a form of preservation ("cure": preserve (meat, fruit, tobacco) by salting, drying and so on—*Concise Oxford Dictionary*). Thus the role of nitrite is not only as a precursor in pigment production but also in development of the typical flavours of cured meat¹ and in microbiological stability. In particular, nitrite may be essential for the inhibition of germination and outgrowth of spores of *Clostridium botulinum*. The statement that "there is considerable doubt about the viability of some cured meats as a culture medium for the spores" is surely without foundation. Concentrations of sodium chloride which when used alone are necessary to inhibit the growth from spores of *Cl. botulinum*, range from 4 to 5% for type E and from 8 to 10% for types A and B. With modern consumer requirements for low salt bacon and meat products, on purely organoleptic grounds, the level of sodium chloride normally used in cured meats ranges normally from 3.5% to 5% on the aqueous phase. In such products, toxin production by *Cl. botulinum* can occur unless adequate nitrite is present also in the product. The amount of nitrite required to inhibit germination and outgrowth of the spores is dependent upon many factors including the pH value, the salt content and the degree of heat process (in the case of canned hams) which is given to the product. It is also dependent upon the number and type of spores of *Cl. botulinum* present². The microbiological stability of pasteurized cured meats may also be influenced by the production of an as yet unidentified antimicrobial agent developed from nitrite³.

The statement that meat was involved in only one case of botulism (*sic* in the USA?) during the period 1950 to 1963 is probably correct. It should be recorded also that no outbreaks of

botulism caused by consumption of cured meat products have been recorded in the UK during the present century. However, in France there were sixty-six outbreaks of botulism affecting some 131 persons during the period 1956–1970⁴. Of these, the majority were attributed to consumption of home-cured ham. It is pertinent to note that residual nitrite was not detected in some of the French hams examined (M. Sebald, personal communication, 1971).

Furthermore, in his assessment of the reported controversy over the potential nitrosation in the stomach of secondary amines of dietary or other origin, your correspondent has failed to recognize the paramount importance of the structure of the amine to the outcome. For instance, Dr Mirvish⁵ of the Eppley Institute, University of Nebraska, has found a 185,000-fold difference in the rates of nitrosation under optimal conditions between the weakly basic piperazine and the strongly basic piperidine. This is reflected in the lack of tumour formation after concurrent feeding of nitrite with a strongly basic amine such as dimethylamine⁶. Whether or not the amines present in foodstuffs or administered as drugs do actually nitrosate in the stomach with the low levels of nitrite available in foodstuffs or present normally in the saliva of the individual must await the outcome of current research, taking account of other reactions competing for the available nitrite.

Naturally your Washington correspondent has dealt exclusively with research, opinions and legislation in the western hemisphere. In so doing, he has had no opportunity to include the extensive programme of research on the role of nitrite in the preservation of meat proceeding at this and other laboratories in the UK and other European countries, particularly Germany.

Yours faithfully,

B. JARVIS

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¹ Cho, I. C., and Bratzler, L. J., *J. Food Sci.*, 35, 668 (1970).

² Roberts, T. A., et al., *Ann. Rpt. Meat Research Inst.*, 1970–71, 77 (1972).

³ Ashroth, J., and Spencer, R., *J. Food Technol.*, 7, 111 (1972).

⁴ Sebald, M., *Bull. Acad. Nat. Med.*, 154, 26 (1970).

⁵ Mirvish, S. S., *Proc. Joint Meeting on the Analysis and Formation of Nitrosamines organized by the International Agency for Research on Cancer, Lyon, and Deutsches Krebsforschungszentrum, Heidelberg* (1971).

⁶ Greenblatt, M., Mirvish, S. S., and So, B. T., *J. Nat. Cancer Inst.*, 46, 1029 (1971).

Our Washington Correspondent replies:

1. The authors question the distinction between the use of nitrite to fix colour in the curing of meats, and its use as a preservative. They point out that curing implies preservation. Clearly, however, the possible distinction is extremely important in the United States because it is being used by the Center for the Study of Responsive Law and others as a central part of their motion for summary judgment in their suit against the Department of Agriculture. The situation is essentially as follows. The 1958 amendments to the Food and Drug Laws provided exemption for those food additives which are "used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to the Meat Inspection Act of 1907". This so-called grandfather clause means that such food additives need not go through the stringent testing and review prescribed by the 1958 amendments. The law suit, however, contends that in the 1920s the Department of Agriculture allowed nitrite to be used in the curing of meat "to fix color", and not to prevent the growth of *Cl. botulinum*. The Department of Agriculture, in its own motion for summary judgment in the case brought by the Center for the Study of Responsive Law, defended use of nitrite largely on the grounds that it prevents growth of *Cl. botulinum* and its toxin. The plaintiffs are therefore claiming that the USDA is defending the additive for a use which has not been sanctioned and which does not come under the grandfather clause. Their contention is that the USDA can only defend use of nitrite as a colour fixer because that is the only sanctioned use in curing meats. (The Food and Drug Administration has, however, approved use of nitrite as a preservative in the curing of chub fish, but this action was taken after the 1958 amendments and is not part of the argument here.) I maintain therefore that the contention is not necessarily a *non sequitur*, and it is up to the courts to decide. It is an important issue in the case.

2. The statement that "there is considerable doubt about the viability of some cured meats as a culture medium for the spores" is based on several different factors. First, spores of *Cl. botulinum* are extremely rare in meat—Mr R. Paul Elliott, Acting Director of the USDA Laboratory Services Division, said in hearings before the Fountain subcommittee, for example (Committee hearings, March 16, 17, 18, 29 and 30, 1971, page 236), "The meat industry is fortunate because the putrefactive anaerobe level is very low. Indeed, the level of *Cl. botulinum* is low almost to the point of extinction." Second, an anaerobic environment is needed for the spores to exist and multiply. Third, types A and B *Cl. botulinum* will not multiply and produce toxins if the meat is refrigerated below 40° F. Another factor which should be borne in mind is that cooking kills the spores and deactivates the toxins produced, and thus products such as bacon and frankfurters do not present a botulism hazard because they are always cooked before eating. It should be noted that the article clearly pointed out that "even those who are most critical of the FDA's regulatory policies for nitrites accept the possibility that it is valuable in preventing botulism from some products". The chief products to come in this category are canned hams and other canned meats stored in anaerobic conditions.

3. I would deny that "the paramount importance of the structure of the amine to the outcome (of nitrosation)" is central to the controversy I outlined in the article. The fact is that laboratory studies have shown mixtures of nitrites and amine drugs to nitrosate in the stomach. While it is true that some amine drugs nitrosate much more

readily than others, it is also a fact that phenmetrazine, a drug used to control appetite, has been found to nitrosate *in vivo* (Greenblatt *et al.*, *Nature New Biology*, **236**, 236; 1972) similarly, aminopyrine has been found to nitrosate *in vivo* (Lijinsky and Greenblatt, *Nature New Biology*, **236**, 178; 1972) and oxytetracycline, aminopyrine, tolazamide and piperine have all been found to nitrosate with high yield in acidic conditions in the laboratory (Lijinsky *et al.*, *Nature*, **239**, 166; 1972). Therefore, to say, as the authors of the letter seem to, that because some drugs do not nitrosate there may not be much of a problem, I think is a wrong attitude to take. It should be noted that the article carefully mentioned that the FDA is not convinced that nitrosation takes place in the stomach, and that the suggestion "is being hotly debated". One other point that is worth noting is that there is a very tricky question of whether or not nitrites, which are not carcinogenic in themselves, are covered by the Delaney Amendment if they are found to lead to the formation of carcinogens in the stomach. If indeed the Delaney Amendment should be interpreted in such a way—and there seems to be a controversy about it—then the structure of the various amines will be totally beside the point. If some amines nitrosate in the human stomach, and the Delaney clause is invoked, then nitrites will be banned without ifs and buts.

4. The above points cover the specific disagreements raised by the authors of the letter, but I think it is worth reiterating the central point of the article—that the FDA has got itself into a bind by not setting sufficient regulations for nitrites (the FDA sets the policy, although the USDA essentially

carries it out in the case of meats). There are, I think, two central points. The first is that the 200 p.p.m. level set by the FDA is totally arbitrary and is not based on any scientific evaluation of risk. The second is that no lower limit is set for nitrites, to guard against botulism from meats, although a level is set for fish: this seems to weaken the case made out for nitrites as a preservative. Another point is that the FDA seems to have been extremely lax in its testing programmes.

Seed Research

SIR,—I am compiling a *Directory* of research work and research workers in Britain currently investigating problems associated with seed germination and seedling establishment. This includes such topics as seed biochemistry, physiology, pathology or, more generally, seed "quality" (whether from an agronomic or food technological point of view) as well as investigation on soil factors affecting field emergence. The intention is to include only those who will be working on their projects for at least two years.

A questionnaire has already been sent to almost 200 people, but it is extremely difficult to know whether everyone engaged in relevant research has been contacted. Could I appeal, therefore, to anyone in Britain who has not received a questionnaire, but who thinks that he or she should be included in the *Directory*, to write to me to ask for one?

Yours faithfully,

T. W. HEGARTY

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